

AMERICAN SOCIETY OF  
CLINICAL PATHOLOGISTS

To all to whom these papers may come:  
GREETINGS! Do it know that  
George N. Papanicolaou

Age of American Pathology

These letters make it known that  
N. Papanicolaou, M.D.  
was elected a  
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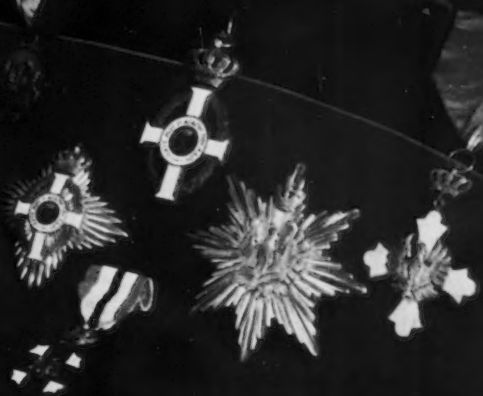


presented to  
George N. Papanicolaou, M.D. by  
The Association of American  
Medical Colleges

For outstanding contributions in the  
diagnosis of malignant diseases and in  
clinical cytologic methods to the progressive  
early diagnosis and detection of cancer.  
At the 105th annual House Meeting of the American  
Association of Medical Colleges, December 28th, 1957

Ca

Bulletin of  
Cancer Progress



*cancer in  
geriatric  
pediatric  
and  
general practice*

The family doctor is in the strategic position of being the first physician to see the majority of cancer patients. His greatest contribution to the control of cancer, early diagnosis, rivals those of the surgeon and radiologist. He has always been active in case-finding among young and middle-aged adults; but his index of cancer suspicion may sometimes lag among youngsters and oldsters. Pediatrics and geriatrics are given increasing importance in his practice by the present decrease in infant mortality and the increase in life expectancy of the population.

His functions in the control of cancer, though less spectacular than those of the surgeon and radiologist, are no less im-

portant. He urges frequent, complete physical examinations either by himself or at a cancer detection center. These physical surveys include rectal examination, uterine cytologic study in women past 35 and chest x-ray examination of men beyond 40, especially the heavy smokers. Such examinations reveal nearly all the known precancerous lesions—leukoplakia, keratoses, moles, fibrocystic mastitis, kraurosis vulvae, cervicitis, cervical erosion and polyps of the cervix, rectum and colon.

Having made a tentative diagnosis of cancer, he urges the patient to undergo confirmatory tests and treatment.

Throughout therapy he acts as liaison between the patient and the surgeon or radiologist, establishing a friendly relationship which supports the patient physically and psychologically.

When the cancer is incurable, he follows the patient through the various artifices of palliation for relief of pain and emotional disturbance. By giving more time and interest to the terminal patient than the surgeon usually can, the family doctor eases the distress and ensures "a gentler passage to the grave."

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*Cover—*

Some of the numerous honors—awards, prizes, scrolls, diplomas, certificates, orders, medals, academic hoods and honorary fellowships—so deservedly bestowed upon Dr. Papanicolaou by medical and scientific, governmental and voluntary organizations in this country and abroad.

The Cross of Grand Commander of the Royal Order of Phoenix was presented personally by King Paul of Greece.

Particularly appropriate and symbolic

of his many victories over various forms of cancer is the replica of the Winged Victory of Samothrace—Lasker Award, 1950, of the American Public Health Association, for his outstanding contributions to research related to cancer.

This statue was set up by Demetrius Poliorcetes in the fourth century B.C. on an island of Dr. Papanicolaou's native Greece to commemorate a naval victory. It was discovered on Samothrace in 1863 and is now in the Louvre.



GEORGE NICHOLAS PAPANICOLAOU, M.D., PH.D.  
EMERITUS PROFESSOR OF CLINICAL ANATOMY  
CORNELL UNIVERSITY MEDICAL COLLEGE

FATHER OF EXFOLIATIVE CYTOLOGY

AUTHOR OF *Atlas of Exfoliative Cytology*  
BORN MAY 13, 1883

The American Cancer Society joins his many students and friends throughout the world in greeting him on the seventy-fifth anniversary of his birth and in wishing him many more years of productive work in the science he originated and developed during the past half century.

# NEWSLETTER

MAY-JUNE, 1958

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On a science editors' tour of 12 cities -- Washington, New York, Philadelphia, Boston, Buffalo, Chicago, Madison, Minneapolis, San Francisco, Los Angeles, Houston and New Orleans -- cancer scientists of 32 institutions were interviewed. Many of these investigators believe that at least some types of cancer may yet be controlled by immunological procedures. Search for vaccines and antigens effective against cancer is being intensified. Some of the reports of the current laboratory and clinical investigation in immunology, viruses and lymphomas follow.

Moore and Southam (Memorial), in collaboration with investigators at Ohio State University, have shown that Memorial's cancer patients have decidedly less resistance to grafts of cultured human cancers than healthy prisoners of Ohio State Penitentiary. The tumors grew for a considerable time in some cancer patients, and in some cases had to be excised. The recipient's immune response increased with each successive transplant -- even in some cancer patients and even when tumors of different types were used.

Toolan (Memorial) has successfully grafted human embryonic skin to cancer patients in a few cases.

Grace (Roswell Park), using the Schultz-Dale technique (anaphylactic spasm of uterine horns in response to an antigen), has shown a qualitative difference between tumor tissue and normal neighboring tissues in one-half the experiments. It was also shown that cancer patients reject skin grafts less readily than do normal individuals. In a few terminal cases autotransplants of the patient's tumor grew, but usually these transplants were rejected. Fogh (U. of Calif.) produced tumors by transplanting human amnion cells cultured in vitro into cortisonized rats.

Kirschbaum (Baylor) reported that urethane increases the leukemogenic potency of estrogens sixfold and of roentgen ray by a substantial factor. The three agents act synergistically. Thigh shielding and marrow infusions did not prevent leukemia induced by urethane; but shielding of the thymus did. Methylcholanthrene reduced by one-half the

(Continued after page 108)

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ARTICLES IN *CA* ARE INDEXED IN CURRENT LIST OF MEDICAL LITERATURE AND QUARTERLY CUMULATIVE INDEX MEDICUS, AND SOME ARE ABSTRACTED IN CHEMICAL ABSTRACTS, BIOLOGICAL ABSTRACTS, EXCERPTA MEDICA AND WORLD ABSTRACTS OF MEDICAL LITERATURE.

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# Keeping up

## Precancerous Lesions

Removal or treatment of precancerous lesions is justified in most cases since this decreases the chance of development of cancer in that area. Study of precancerous lesions in regard to all known factors affecting cell division, such as enzyme systems, viruses, hormones, mutagenic agents and tissue organizers may give important information as to the nature of the malignant transformation. However, not all etiologic factors produce morphological changes prior to cancer formation. In many types of neoplasms even an extensive search for such changes may be futile. Studies on experimental animals of the changes preceding development of tumors by application of chemical carcinogens indicate: (1) that in some cases morphological changes similar to those of the human precancerous lesions precede the appearance of malignant tumors; (2) that morphological changes may persist indefinitely without production of malignant change; and (3) that often the malignant change is not preceded by a morphological change. Therefore, the precancerous lesion can not be said necessarily to possess incipient malignant properties. Some cancers are caused by a combination of several systemic and local factors. Theoretically, all precancerous lesions might become malignant if there was sufficient time for the causative factors to act.

*Skoryna, S. C.: The precancerous lesion. [Editorial.] Canad. M. A. J. 78:205, Feb. 1, 1958.*

## Urinary Cytology

The value of cytological study of urinary sediments in the diagnosis of cancer

of the genitourinary tract was appraised in a group of 2,829 cases. In 212 cases of carcinoma of the bladder, ureters or renal pelves, 61.7 per cent were correctly interpreted by examination of smears of the urinary sediments. In the group of renal cancers only 8.3 per cent were correctly diagnosed by this method. Most of the urine specimens were from the bladder; better results would have been obtained with catheterization specimens from the upper portions of the urinary tract. Cytological examination of urinary sediments revealed only 15 per cent of the prostatic carcinomas. Approximately 90 per cent of the negative reports were correct; and there was approximately one per cent of false positive reports. In 60 per cent of the over-all cases correct cytological interpretations were reported upon examination of the first specimen. Examination of repeat specimens raised this percentage in the group of bladder tumors to 77.5. By this cytological method a number of carcinomas in situ of the bladder and renal pelvis were discovered. This method is also useful in detecting recurrences of genitourinary cancers after resection. Detailed laboratory procedures are presented.

*Foot, N. C.; Papanicolaou, G. N.; Holmquist, N. D., and Seybolt, J. F.: Exfoliative cytology of urinary sediments: a review of 2,829 cases. Cancer 11:127-137, Jan.-Feb., 1958.*

## Cancer Research in the British Empire

The 34th annual report of the British Empire Cancer Campaign, a volume of nearly 600 pages, is reviewed. The work reported is classified as follows: (1) studies of human tumors and clinical investigations, (2) radiology and (3) carcinogenesis, environment, viruses, bio-

# with Cancer



chemistry of tumors, enzymes, hormones, nucleic acids, cytology, steroids, immunology, chemotherapy, tissue culture and genetics. Concerning the failure of British workers to confirm Wynder's results, it is stated that lack of carcinogenic response of some mouse skin to tobacco tar does not *prove* it to be inactive on human lung tissue. A symposium on estrogen methodology concluded that the idea of a specific urinary steroid excretion pattern associated with neoplastic disease is not supported by the experimental evidence. Xenon-133 is being studied as a radioactive substitute for the x-ray tube. Good radiographs of fractures can be obtained with exposures of only a few seconds using sources of high activity. Cobalt-60 and cesium-137 units are being used more and more in therapy. Much attention was given to low levels of radiation applied to large populations, and to long-latent carcinogenic effects of clinical irradiation. Cytological diagnosis, especially of cervical carcinoma in situ, is coming into wider use. Cancer registers established in various geographical locations are gradually accumulating epidemiological information of value in the study of the etiology of cancer. The reviewer considered the least formal report to be the most readable—that by the late Sir Ernest Kennaway of his visit to the United States to discuss tobacco and lung cancer with Wynder and others.

*Anon.: Progress of cancer research. Nature 180: 1312-1314, Dec. 14, 1957.*

## Preventive Surgery

The only instance where minimal surgery may be used in cancer care is for

removal of precancerous conditions—leukoplakia; polyps (particularly of the colon and rectum); junctional nevi in areas of irritation, such as the perineum and hands and feet; adenocystomas of breast and thyroid; gallstones; abnormal nodules of the skin, subcutaneous and soft tissues; and chronically infected or ulcerated burn-scar areas. Circumcision is one of the best examples of preventive surgery. Gastric ulcers, if unhealed, require removal; and patients with pernicious anemia should be carefully watched, because they are more prone to develop gastric cancer than is the average person. An undescended testicle is twenty times more prone to malignant change than a normal testicle.

*Clark, R. L., Jr.: Surgical treatment of the cancer patient. Am. Surgeon 23:336-345, April, 1957.*

## Etiology and Histology of Lung Cancer

Kreyberg in 1955 (abstract in *CA* 6:152, 1956) reported two histological groups of lung cancers: one, embracing squamous-cell, large-cell and small-cell carcinomas (including oat-cell carcinoma), related to tobacco smoking in men, and the other, embracing adenocarcinomas, bronchiolar (alveolar-cell) carcinomas and various grades of adenoma and salivary-gland type tumors (including cylindromas), unrelated to tobacco. The histology of the cases reported by Doll and Hill in 1952 (abstract in *CA* 4:149, 1954) was restudied by one pathologist without a knowledge of the sex and smoking habits of the patients and the various types of lung cancer correlated with the amount of tobacco consumed. In men, there was a close relationship of the

daily tobacco consumption to the first histological group of lung cancers, but only slight, if any, to the second group. No definite conclusion could be drawn from the too small number of women in the study. These findings, conforming to those of similar studies in Norway, the United States and elsewhere, support the hypothesis that differing etiological factors can produce tumors of different histological types in the same anatomical site. Among the data developed in the study was the fact that the risk to the smoker consuming 25 gm. (1 gm. per cigarette) of tobacco a day is more than 25 times that to the nonsmoker.

*Doll, R.; Hill, A. B., and Kreyberg, L.: The significance of cell type in relation to the aetiology of lung cancer. Brit. J. Cancer 11:43-48, March, 1957.*

#### Limited vs. Extensive Surgery

There is place for a graded approach in the treatment of cancer. Most surgeons treat cancer of the lip by wide local excision, reserving neck dissection for patients in whom metastases are present or later appear. Melanomas are often similarly treated. There is no statistical proof that prophylactic resection of regional nodes is more likely to control the cancer than is therapeutic resection soon after regional metastases are palpable. Papillary thyroid cancer without palpable nodes is an example of a cancer in which an acceptable attack is resection or destruction of the primary tumor. Cancers low in the rectum that appear to be limited to the mucosa and are quite small can be successfully treated by electrocoagulation. If they are not thus controlled, a combined abdominoperineal resection still can be done. Similar graded treatment can be applied to small cancers of the tongue and gingival margins, to cancers in situ of the cervix and to Stage I cancer of the breast without palpable nodes—all well adapted to local eradication, to accurate follow-up and hence to graded treatment. Much of the mortality and morbidity of extensive operations indiscriminately applied can be avoided by such treatment. When a limited operation has a good

chance of controlling a disease, and when this limited operation does not jeopardize the success of a subsequent more extensive one, it may be best to try the simpler operation first.

*Crile, G., Jr.: A graded approach to surgical treatment. [Editorial.] Am. Surgeon 23:93-94, Jan., 1957.*

#### Arsenic in Cigarettes

The arsenic content of American-tobacco cigarettes increased from 12.6 micrograms in 1932 to 42 micrograms in 1951. Since that time the arsenic content has fallen considerably owing to the gradual abandonment of arsenical insecticidal sprays by the growers in this country. Of the arsenic in a cigarette, 7 to 18 per cent is volatilized in smoking, 60 per cent remains in the ash and about 25 per cent in the stump. Arsenic content of 39 brands of cigarettes from 18 countries during 1948 to 1956 varied from nil in Turkish tobacco to more than 100 micrograms arsenic trioxide per gram in a popular British brand.

*Bailey, E. J.; Kennaway, E. L., and Urquhart, M. E.: Arsenic content of cigarettes. Brit. J. Cancer 11:49-53, March, 1957.*

#### Host Factors in Lung Cancer

In 210 autopsies of lung cancer cases the pathological findings were correlated with the environmental and the host factors. More than 90 per cent of the men with epidermoid lung cancer had significant prolonged exposures to suspected respiratory carcinogens: cigarette smoking—57 per cent, occupational—37 per cent. Six per cent had asthma or bronchiectasis. In women with lung adenocarcinoma, environment seemed to be of minor importance to the prior hyperestrogenic state with ovarian stromal hyperplasia followed by pituitary-adrenocortical alteration and an inferred endocrine hyperactivity. Extrinsic carcinogenic factors were considered to be generally relatively more important in the background of lung cancer in men than the active peculiarities of individual hosts.

*Sommers, S. C.: Host factors in fatal human lung cancer. A. M. A. Arch. Path. 65:104-111, Jan., 1958.*



a glance . . .

**one-minute abstracts of the  
current literature on cancer in  
geriatric, pediatric and general practice . . .**

### **Disease and Age**

Chronic disease in an aging population is a problem facing all physicians in the United States. It is often difficult to distinguish between the natural processes of aging and disease. Too many physicians take the attitude that aging is inevitable, so why do anything about it. This is particularly dangerous in regard to cancer because if this disease is to be minimized in importance the whole cancer detection program is adversely influenced. There may be a mental block not only on the part of the patient, but also the physician so that diagnosis of cancer might be arrived at by exclusion of all benign causes rather than by first suspecting the most lethal and important cause.

The present increasing life expectancy indicates that in 1975 the average length of life will be 71 years instead of the present 68. This will shift the general practitioner's interest to a still greater extent to the older age group. Most forms of malignant disease, with the possible exception of cancer of the ovary or testicle, increase in incidence with age so that we will see more and more cancer and will have to revise our thinking in regard to the use of surgery in the older age group. We are no longer justified in withholding operative treatment from these patients. It is not justifiable to sit idly by assuming

that an associated degenerative disease will kill the patient before cancer catches up with him. For example, an older patient with cancer of the stomach may stand a better chance in resection than some of the younger patients because the tumor may grow at a slower rate and metastases occur later and less readily in the older patient. Similarly, cancer of the rectum often responds better in the older than in the younger patient. In cancer of the breast or vulva, the results may be even more rewarding. The real problem is proper selection of suitable patients for operation. And operations should be designed to be curative rather than palliative when possible. More and more resections or primary gastrointestinal lesions are being done rather than the short-circuiting palliative operation, even in the presence of a few metastases. In selection of patients the cardiovascular-renal impairment is more important than the chronological age of the patient. There is something tough about patients who live to be 70 or 80 years old. The older patient properly prepared and managed comes through the operative procedure just as well as the younger patient. There is no place for the defeatist attitude in connection with the surgical treatment of the aging. Early diagnosis of cancer is just as important in the older patient as in the younger group. The patient should be per-

suaed that something can be done for him in all phases of malignant disease. Care must be taken not to increase the patient's fear of malignant disease. Not everyone who smokes or is exposed to smog will get lung cancer. The importance of hormones as factors in the causation of cancer is often exaggerated in the mind of the patient.

Ryder, C. F.; Ropes, M. W.; Parsons, L.; White, P., and Monroe, R. T.: Symposium on disease and aging. *J. Am. M. Women's A.* 12:157-170, June, 1957.

### Tumors in Childhood

Cancer should always be considered in the differential diagnosis in children because it is exceeded only by accidents and pneumonia as a cause of death. Early symptoms of cancer in childhood are often vague and simulate symptoms of benign diseases. The adult type of anemia, pain and loss of weight are usually absent. Cancer should be thought of in all cases of vomiting without nausea, recurrent dizziness, headache, anorexia, partial loss of vision, painless mass in any location, persistent large lymph nodes and bone pain in one extremity. Early recognition and treatment of cancer in the child is made possible only by an awareness of the symptoms, by frequent examinations and by teaching parents to seek medical help for unusual swellings or pain in their children. The brain is the most common site of malignant tumors in children. Bone tumors are the second most frequent. Genitourinary tumors account for almost half the deaths from cancer in children under five years of age. Neuroblastoma is one of the most common tumors of infancy and occurs almost exclusively in that age group. Leukemia is the third most frequent neoplastic condition seen in pediatric practice. The acute form is more common than the chronic in children. The usual symptoms are pallor, loss of weight, sore mouth, bleeding gums, bone destruction, petechia and purpuric spots. Joint and bone pains are common early symptoms and are often mistaken for rheumatic fever. Hodgkin's disease is the most common type of malignant lymphoma occurring in children. All physicians should

remember that cancer is common in children and that early recognition and treatment give the best chance for recovery.

Henry, R. L.: *Neoplasms in childhood. J. Arkansas M. Soc.* 54:362-364, Feb., 1958.

### Prevention of Tumor Recurrence

Motivated by the high mortality rate in patients with malignant tumors—82 per cent in adults and still higher in children—the authors sought a method for increasing the natural antitumoral resistance. Immediately after primary surgical or radiation therapy the authors administered those vitamins which do not increase but rather decrease the growth of tumors in animals, and in addition gave their patients cerebrosides, organ extracts and certain mineral salts. This method prevented recurrence in 30 adults for three years. One child of five years with a retroocular and intracranial glioma, nine years after removal of the tumor, was still without recurrence, although the surgeon could not give assurance of non-recurrence on account of the uncertain boundaries of the tumor. Using the method of Leopold (Cologne) of increasing antitumoral resistance by administration of precise courses of insulin, the present authors obtained good results in about 50 per cent of cases not responding to classical methods. Since this technique can cause resorption of macroscopic tumor masses it is reasonable to suppose that it can also destroy microscopic neoplastic nests which cause recurrences. This harmless prophylactic treatment should be used in all cases of malignant tumor in adults and children.

Kousmine, C., and Strojewski, M.: *Conception nouvelle du traitement des maladies tumorales. Prophylaxie de la rechute. [New concept of the treatment of tumors. Prevention of recurrence.] Ann. Paediat. (Basel)* 190:188-189, Mar., 1958.

### Leukemia in Children

Ninety cases of acute leukemia in the Moscow Pediatric Institute are reviewed. In the past 15 years the incidence of the leukoses in children has increased. There are two peak age periods for the incidence of leukemia—from 3 to 6 and from 9 to

12 years, and the incidence is greater in March and September than in other months. Immature leukocytes in peripheral blood are indicative of leukosis even when leukocyte count and hemoglobin are normal. To ensure early diagnosis a careful history is necessary, and frequent blood counts and sternal marrow examinations should be made. Errors in early diagnosis are frequently made. Symptoms of leukemia in order of frequency are lymphadenopathy, pain in bones and joints, joint swelling often mistaken for arthritis, tonsillitis, asthenia, lethargy, hemorrhage, nausea, pneumonitis, headache and fever.

*Mukhamedzyanova, G. S.: Early symptomatology and diagnosis of acute leukemia in children. Paediatrics No. 6, 7-11, June, 1957.*

### Pediatric Tumors

Next to accidents, neoplastic diseases, which include leukemias as well as benign and malignant tumors, stand first among all causes of death in the group from five through fourteen years of age. Most tumors in childhood are congenital. Hence, the process has been active in many instances since prenatal life plus the variable period postnatally before clinical evidence of the tumor. Clinical syndromes may mimic many common diseases of children because of the multitude of anatomic sites which may represent either the primary or metastatic tumor. A child with leukemia may show no important changes in the peripheral blood that will give a clue to the diagnosis for many months. The need for early bone marrow studies in doubtful hematologic disorders is now widely recognized. The proper approach to the diagnostic phase of tumors in childhood requires one to consider invariably the possibility of neoplasm in making a differential diagnosis whether the condition be chronic, subacute or acute. Surgical or radiation therapy show gratifying results in more and more cases. Increasing numbers of children now survive five or more years following therapy for medulloblastoma, retinoblastoma, Wilms's tumor, lymphosarcoma, etc. Chemother-

apy has prolonged the lives of many leukemic children and has been of palliative benefit in other cancers, as lymphosarcoma, reticuloendothelioses, etc. No matter how effective therapy for any disease may be, it will be useless unless initiated before the disease has advanced to a state of irreversibility. The salvage of such children will increase significantly when earlier diagnosis of juvenile cancer is accomplished.

*Dargeon, H. W.: Tumors in childhood. New York J. Med. 58:402-403, Feb. 1, 1958.*

### Individuality of the Older Patient

In the treatment of any patient his individuality must be considered. This is particularly important in treating the older patient who exhibits a wider range of symptoms and disorders. In the child and young adult the clinical state usually approximates the classic textbook picture and justifies a single diagnosis of single etiology. In the older patient the disorder is more often multifaceted and multifactorial. This multiplicity of factors can not be ignored in the older patient. Relatively small factors may prove to be of major importance in the older patient. Several examples of this are presented:

A 59-year-old spinster school teacher had been told she was incurably ill with cirrhosis of the liver, diabetes, hypertension and heart failure. She had retired, changed her residence and given up in despair. Her previous history disclosed a hysterectomy for uterine fibroids and a simple mastectomy for a nodule in the right breast, which had been performed when she was 37 years of age. The nodule had included a small carcinoma *in situ*. She was thoroughly frightened of her illness and of doctors. She was given reassurance and cooperated in a complete clinical study which revealed a retroperitoneal lipomyxosarcoma which was removed at operation. Her medical recovery was unimpeded by this discovery. She emerged from a short retirement with a remarkable change of attitude and found employment in an advertising firm for three years when a carcinoma of the left

breast was discovered. This was removed successfully although regional nodes were involved. She was inconvenienced but not disabled by moderate lymphedema. A recurrence of the tumor in the left supraclavicular fossa was treated by radiation and a moderate hypertension was treated symptomatically. She lived to the age of 70 despite four independent tumors, a complicating unusual nephropathy and chronic hypertensive cardiovascular disease.

Diagnosis is not synonymous with disability and chemical analysis alone does not identify a state of health or carry a prognosis. The great value of results of modern scientific methods of clinical examination is that they assist in estimating the functional reserves, which may be called upon under adverse conditions and this aids in assessing the individual's potential limitations for work, recreation, disease or restoration.

Landowne, M.: *The singularity of the (older) patient.* Maryland M. J. 6:683-689, Nov., 1957.

### Cancer in Childhood

Eighty per cent of cancers in children and 7 per cent in adults arise in the nervous, lymphatic, hemopoietic and urinary systems. Six per cent of cancers in children and 80 per cent in adults arise in the alimentary, genital and respiratory systems. In 15 of 28 patients with neuroblastoma, regression of the tumor followed administration of vitamin B<sub>12</sub>, four of these died in relapse and one died of intercurrent poliomyelitis. Ten patients survived, with tumor regression maintained, for from 1 year and 6 months to 6 years and 6 months. Vitamin B<sub>12</sub> caused more than 50 per cent of neuroblastomas to regress. In the first year of life 100 per cent of all neuroblastomas regressed.

McNab, G. H.: *Cancer in childhood.* Quart. Rev. Pediat. 13:18, Feb., 1958.

### Cancer in a General Practice

During one year the author saw 1146 patients; in 12, an original diagnosis of cancer was made. These together with

previously diagnosed and treated patients gave a total of 60 cancer cases. Two patients were asymptomatic but with blood pictures of leukemia. Two had well-controlled metastatic cancer and nine were terminal. The remaining 47 had no evidence of recurrence or metastasis. Twenty-seven of the 60 cases were cancers of the breast. Two of these were patients with metastases who were kept active and comfortable for more than a year with hormone therapy. Eleven of the 27 were five years or more without metastases, and 14 were apparently well less than five years after mastectomy. Of 18 patients with cancer of the large bowel, seven were well more than five years after operation, nine, less than five years, and two died. Of the other 13 patients with cancers of other sites, five died and eight were without evidence of disease. The nine terminal patients, all more than 69 years of age, were kept comfortable with sedatives, chlorpromazine, corticoids and other hormones and minimal narcotics. Only two of the terminal patients occupied hospital beds for more than thirteen days. Home nursing care by devoted families minimized excessive occupancy of community hospital beds. The general practitioner must accept the responsibility for early diagnosis, for guiding the patient wisely through his surgical and radiologic treatment and for the palliative therapy and human sympathy required through the final stages. His role in the control of cancer, though not dramatic, is essential.

Root, M. T.: *The general practitioner's place in the cancer program.* Cancer News 12:14-15, Winter, 1957.

### Intestinal Polyps in Children

It has often been stated that polyps of the rectum and colon in children almost never undergo malignant transformation. Although relatively rare in children, polyps of the colon and rectum occur frequently enough to be considered as a cause of painless, intermittent rectal bleeding. Protrusion of a mass from the anus often indicates the diagnosis. Digital and proctosigmoidoscopic examinations are confirmatory in approximately three-

fourths of patients. Polyps located beyond the reach of the proctosigmoidoscope are visualized by double-contrast, roentgen-ray studies. Approximately 75 per cent of rectal and colonic polyps are single, pedunculated and located in the rectum. Recommended treatment is excision with cold biopsy forceps or with an electrothermic snare through the proctosigmoidoscope. For polyps above the sigmoid colon and for sessile polyps above the peritoneal reflection, transcolonic excision with ligation of the pedicle is recommended. Follow-up is important. No evidence of overt malignant transformation was seen in the authors' patients. Potential malignant transformation in polyps of the rectum and colon of children is probably no greater than in the normal mucosa of the rectum and colon.

*Horrelleno, E. G.; Eckert, C., and Ackerman, L. V.: Polyps of the rectum and colon in children. Cancer 10:1210-1220, Nov.-Dec., 1957.*

### **Heredity and Wilms's Tumor**

A family is reported in which in three generations four children had died and one was operated on all between the ages of 1 and 3 years with diagnosis of renal or abdominal tumor. In one case the diagnosis of Wilms's tumor was verified, in two cases the clinical diagnosis was renal tumor and in two cases, abdominal tumor. Diagnostic points indicated that all five of these patients had Wilms's tumors and that this family has a hereditary predisposition to this tumor. Five previous Wilms's tumor families have been reported. Renal tumors are considered to be the second commonest type of malignant tumor and the most common type of abdominal malignant tumor in infants and small children.

*Strom, T.: A Wilms' tumor family. Acta Paediat. 46:601-604, Nov., 1957.*

### **Tell the Patient?**

The modern physician takes pride in exposition. He avoids dogmatic authoritarianism. He feels that his prime respon-

sibility is to teach the patient all that he can comprehend about his illness; exposition, not dictation, is his concern. If the physician has some skill as a teacher, or even merely patience, he will have little difficulty in translating essential technical details for an individual whose attention should be well focused. And this participation of the sick person is not confined to the management of his treatment; it is often very important in the analysis of his case, as well.

*Atchley, D. W.: The changing physician. The Atlantic 198:29-31, Aug. 1956.*

### **Leukemia and Mongolism**

The coincident occurrence of acute leukemia and mongolism—both of unknown pathogenesis and rare—in numbers far exceeding the statistically expected frequency suggests a biologically significant relation between the two conditions. Two of 56 patients under 15 years of age with bone marrow diagnosis of acute leukemia had definite stigmata of mongolism. Another clinic reported four cases of acute leukemia among 255 mongol children. Still another group, finding five cases of coincident mongolism with acute leukemia—four within a one-year period—calculated the chance coincident occurrence of these two conditions as 1:10,000,000, and that one case would be anticipated in 50 to 100 years in their state of Minnesota. Mongolism is attributed to teratogenic factors acting on the fetus between the sixth and ninth weeks. The same or other deleterious factors of stress may also trigger the maldevelopment of the blood dyscrasia. This conjecture is supported by the fact that 6 of the twenty instances of leukemia occurring concomitantly with mongolism were of the congenital type. Variations in age when leukemia becomes apparent is a simple reflection of the variability of the latent period. The damaged tissues may retain increased susceptibility to leukemogenic influences for varying periods.

*Sutow, W. W., and Welsh, V. C.: Acute leukemia and mongolism; report of two cases. J. Pediat. 52:176-181, Feb., 1958.*

## Radiation in Neuroblastoma

Neuroblastoma is one of the few malignant tumors in which aggressive therapy is justified regardless of the extent of its dissemination. Occasionally children with widespread metastases may be cured. Seven of 19 patients have lived for from 10 to 76 months, and five of these survived for more than three years following radiation therapy. All of the seven surviving patients were less than 17 months of age when therapy was begun, and the average age of those who died was 42 months. Two of the surviving patients had histologically verified metastases, one of liver and one of bones. Radiation may act by influencing the process of maturation and spontaneous regression or differentiation into a benign ganglioneuroma, and this process has been enhanced by nitrogen mustard, cortisone, antifolates and surgical trauma from partial removal or biopsy. Regardless of the mechanism of action, radiation, employed in the presence of extensive disease and metastases, saves a significant number of patients.

Seaman, W. B.: Radiation therapy of neuroblastoma. *Radiology* 68:1-8, Jan., 1957.

## Neurologic Factors in Leukemia

Although neurologic signs and symptoms are not frequently encountered in the course of leukemia, pathologic changes in the nervous system are frequently seen at necropsy. Three cases of acute lymphocytic leukemia with neurologic manifestations—clinical signs and spinal fluid findings—resembling those of acute bacterial meningitis are reported. Among the neurologic manifestations of leukemia previously reported are cranial nerve palsies or anesthetics, facial paralysis, fever, delirium, stiffness of the neck, positive Kernig and Brudzinski signs, paraplegia, polyradiculitis, transverse myelitis, epileptiform seizures, paresthesia of legs and optic neuritis. Examination of the cerebrospinal fluid of leukemics is seldom made. Even in the absence of neurologic signs or symptoms such examination, including leukocyte count and sugar estimation, may

be useful. When neurologic symptoms appear in leukemia the process is usually terminal. Further study of the glycolytic activity of leukemic and normal leukocytes is suggested.

Gilbert, E. F., and Rice, E. C.: Neurologic manifestations of leukemia; report of three cases in children simulating acute bacterial meningitis. *Pediatrics* 19: 801-809, May, 1957.

## Wilms's Tumor

Wilms's tumors have usually reached a diameter of 5 to 10 cm. before they are discovered, because of their deeply located site of origin. The finding so alarms the parent that there is little delay in seeking medical attention and investigation. This tumor is second only to leukemia in the age group under five years, and is of particular interest because some cures are possible. A study of the data concerning 422 patients with Wilms's tumor showed 340 of them with the necessary chronological information upon which to base the postulate that following nephrectomy the patient is at a risk of tumor recurrence for a period equal to his age at the time of diagnosis plus nine months. If the patient lives beyond this period without recurrence, he should be beyond risk of recurrence. Seventy-three of the 340 patients survived beyond the period of risk without recurrence and in only two was recurrence deferred beyond this point. This postulate offers a basis for prognosis in individual cases. As treatment, emergency operation and immediate postoperative radiotherapy are recommended. Preoperative irradiation reduces the size of the tumor and facilitates surgical removal. Postoperative irradiation destroys residual cancer cells in the tumor bed, and need not damage cord, soft tissues, bowel or blood-forming organs if the skin dose is kept to an estimated three-fourths of tolerance. If there are no distant metastases, cure is possible if the primary lesion can be completely removed and the residual cells destroyed by irradiation. Cure rate in this group of 340 patients was 21.5 per cent.

Collins, V. P.: The treatment of Wilms's tumor. *Cancer* 11:89-94, Jan.-Feb., 1958.

# The Role of the General Practitioner in the Diagnosis of Early Cancer

*John G. Walsh, M.D.*

Regardless of the many advances in diagnostic procedures and technical skills in the treatment of cancer there exists a discouraging observation in the reports of most cancer authorities. That unpleasant fact is the realization that the past twenty-five years have not brought about a remarkable lowering of the mortality rate from cancer. Since no specific cure, preventive vaccine or miracle drug has yet been discovered to combat this disease the medical profession must still rely upon early diagnosis as the means toward solving this major problem in order to increase materially the survival rate of cancer patients. The cure is directly proportional to the prompt diagnosis and earliest possible treatment by accepted surgical or radiological procedures.

It is not enough to rely upon the patient's interpretation of the much publicized "seven common danger signals of cancer" for the simple reason that a patient with early cancer may be asymptomatic for many months before a subjective sign presents itself.

The modern general practitioner is well equipped to conduct a thorough physical examination to detect early cancer in the asymptomatic patient.<sup>1</sup> Since family physicians care for the majority of the population and are responsible to a great degree for referrals to specialist consultants, the success of a program for earlier diagnosis of cancer is dependent upon the interest, alertness, and thoroughness of family physicians in performing physical examinations. Although there are some enthusiastic reports from cancer detection centers, a thorough examination by the private physician is most desirable by virtue of the traditional patient-doctor relationship, less delay in appointments and lower cost from the standpoint of the patient and the "detective." This recommendation is endorsed and publicized by the American Cancer Society.

<sup>1</sup>2901 Capitol Ave., Sacramento, Calif.

The lay public has to a great extent accepted the program of a periodic health checkup, but all too often the patient has been disappointed by the lack of thoroughness of the examining physician. This subject cannot be treated lightly when we know that 450,000 citizens of this country will develop cancer this year, and only one-third will be cured leaving two-thirds to die of the disease within a five-year period. Only by earlier detection will some of this two-thirds group be cured.

Family physicians in increasing numbers are urging patients forty years of age and over to plan on yearly physical examinations. Although cancers can occur at any age the vast majority occur in middle life. Thus, the age groups from forty to sixty must be stressed from a percentage standpoint.

(Figure 1 shows the relative incidence of cancer sites in males and females.) The physician must think in terms of the incidence of cancer and not in terms of mortality figures. He thereby will develop a greater interest in the early diagnosis of the disease instead of a morbid fear of finding a far advanced, incurable lesion. The psychological approach to this disease must be optimistic on the part of the physician as well as the patient.

## History

A careful history is most essential in order to uncover clues to unsuspected malignant lesions. A man forty-five years of age may not attach much significance to a chronic "cigarette cough" but the physician must be suspicious of this symptom in the male approaching the sixth decade of life. Cancers of the gastrointestinal tract likewise may be suspected by the history. A patient with longstanding indigestion is not aware of the possibility of an achlor-

FIG. 1. ORDER OF INCIDENCE OF CANCER SITES

Men	Women
1. Skin	1. Breast
2. Lung	2. Cervix
3. Prostate	3. Intestines
4. Stomach	4. Skin
5. Intestines	5. Endometrium
6. Rectum-Sigmoid	6. Stomach
7. Bladder	7. Rectum-Sigmoid
8. Leukemia	8. Ovary
9. Lips	9. Leukemia
10. Pancreas	10. Other Sites
11. Esophagus	
12. Other Sites	

hydria that will foretell the onset of a gastric cancer. Lesions of the colon may produce longstanding symptoms of flatulence, indigestion, or change of bowel habits that are not significant to the average patient.

Only through a careful routine case history will cancer be suspected in the so-called inaccessible sites that can be discovered by proper x-ray diagnostic procedures. The most common sites will be the lung, stomach and colon. Kidney, brain and bone cancers can likewise be diagnosed only through the aid of radiography indicated following a detailed history.

### Inspection

The second essential step to a complete physical examination for cancer is inspection. This necessitates the removal of all clothing from the patient. Such a suggestion sounds elemental, but all too frequently examinations are conducted on partially clothed patients.

Inspection of the oral cavity may show an area of leukoplakia or atrophy. These findings preexist in the majority of cases of oral cancer and may be considered pre-

cancerous. A laryngoscopic mirror is a valuable aid in the examination of the pharynx, nasopharynx and laryngeal area.

Inspection of the skin may reveal precancerous keratoses or basal-cell carcinomas in the older age groups. The exposed surfaces are the most common sites for such skin lesions. Early total excision will effect a 100 per cent cure. The incidence of the most dangerous skin cancer, malignant melanoma, is reported as 1.5 to 2.5 per cent of all cancers. Prophylactic treatment is indicated when the diagnosis is made of the junctional nevus and compound nevus. These lesions may become malignant. Criteria for total excision and biopsy are: (1) lesions on the palms, soles and genitals, (2) ulceration, (3) those subject to chronic irritation or (4) sudden darkening or increase in size or elevation.

### Palpation

With the advances in mechanical techniques in diagnosis there seems to be a laxity on the part of doctors in utilizing palpation as a diagnostic tool. We now

realize more than ever that only by palpation will certain early cancers be discovered. These include cancers of the thyroid, breast, kidney, uterus, ovary, rectum, testicle, prostate and bone.

Digital palpation of the rectum is an all important part of the examination since half the lesions in the lower bowel can be palpated.

Palpation of the prostate is the only method of finding an early cancer of that organ. Cancer of the prostate ranks third in incidence of cancer in males, and it has been reported that approximately 95 per cent of all prostatic cancers are first diagnosed clinically in the metastatic phase. Examination every six months in men past fifty-five years of age followed by suitable biopsy of suspicious areas is a recommended procedure.

Palpation and self-examination of the breast is the answer to a lower mortality rate from breast cancer in the female. Instructions in the technique of breast examination should be part of every physical checkup of the female. The patient will be impressed to learn that almost one-fourth of cancers in the female are located in the breast and that most of these lesions are first discovered by the patient. The results in survival rate from breast cancer are directly proportional to the early diagnosis, prompt biopsy and treatment.

The Papanicolaou smear<sup>3</sup> technique is available for screening cancer of the cervix and endometrium, but such a procedure is not helpful in early cancer of the ovary which ranks third in incidence of cancer of the female genital tract. Ovarian "cysts" in women past thirty-five years of age should be considered cancer until proved otherwise.

Palpation alone will detect these early lesions.

### **Instrument Aids**

The modern family physician is equipped with simple instruments which can be utilized to diagnose an early cancer. These include the laryngoscope, vaginal speculum, sigmoidoscope and simple biopsy instruments.

A vaginal speculum examination may be negative, but it must be remembered that many carcinomas in situ of the cervix are suspected from the Papanicolaou smear taken from an apparently normal cervix. Adequate biopsy will make a positive diagnosis. The Papanicolaou smear should be utilized in all women who have borne children and routinely in women past thirty-five years of age. Smears at six-month intervals are desirable. It must be remembered that a Papanicolaou smear may be negative in the presence of an obvious invasive carcinoma of the cervix, making a tissue biopsy imperative.

Sigmoidoscopy is probably the most neglected procedure in office practice today. It is also one of the most simple procedures to learn. All patients past forty years of age should have such an examination using the 25-cm. scope after the lower colon has been properly evacuated. Many premalignant and early malignant lesions will be found in the asymptomatic patient. Two-thirds of lesions in the large bowel can be visualized through the sigmoidoscope.

### **Laboratory Aids**

Laboratory aids play an important part in the program for the detection of incipient cancer. The general practitioner has available such tests as urinalysis (including microscopic examination), hematocrit and differential blood count, Papanicolaou smear, stool examination for occult blood and gastric analysis for achlorhydria.

Most general practitioners conduct simple laboratory procedures as microscopic urinalyses, blood counts and blood smears and tests for occult blood in the stool. Physicians close to clinical laboratories utilize such facilities for gastric analysis and stool examinations.<sup>1</sup> The highly skilled procedure of interpreting Papanicolaou smears<sup>3</sup> must be reserved for the clinical pathologist and his specially trained technicians.

Positive findings in any of these laboratory procedures warrant further investigation. The source of occult blood in the

stool or microscopic blood in the urine should be considered cancer until disproved. A positive Papanicolaou smear must be further investigated by tissue examination.

A tubeless gastric analysis<sup>2</sup> as a screening test for achlorhydria has recently been used with enthusiasm. The test developed by Segal and his co-workers is a simple qualitative detection of free hydrochloric acid. Its simplicity makes possible its use as a screening procedure for the detection of achlorhydria in the routine examination of the asymptomatic patient. The reported low incidence of "false negative" tests makes this test justified for use in mass surveys and as part of the routine office procedure especially in men past forty-five years of age.

Achlorhydria or hypochlorhydria indicates the need for gastric x-ray studies at yearly intervals regardless of the absence of symptoms. Since routine x-ray studies on all patients past forty-five years of age are neither practical nor advisable, a roentgenologic screening procedure of selected individuals would result in an increased incidence in the diagnosis of early gastric cancer.

The suspicion of lung cancer in the asymptomatic patient must depend upon the routine roentgenogram until a better procedure comes along. This most fatal of cancers in males can be suspected in the age groups of over forty years especially in heavy cigarette smokers. If one waits for symptoms of cough and hemoptysis the chances are slight that the lesion is early. Hidden symptoms uncovered from the history with suspicious x-ray findings would indicate further specialized diagnostic procedures as bronchoscopy and Papanicolaou smears of the aspirations from the bronchi. Exploratory thoracotomy may be necessary as a diagnostic procedure.

## X-ray Films as Diagnostic Aid

Much has been written recently about the promiscuous use of diagnostic x-ray films and some criteria must be decided upon in selecting the use of such procedures in a cancer examination.

The three inaccessible sites of the body where diagnostic roentgenography may be most helpful are the lung, stomach and colon.

Periodic photofluorographic films of the chest in men past forty-five years of age are recommended by many authorities.

Periodic gastric x-ray examination in patients with achlorhydria or hypochlorhydria will reveal some early cancers in such a series of cases.

A barium enema with an air contrast study is indicated when benign polyps are discovered on sigmoidoscopy, when the history suggests a change of bowel habits or when occult blood is found in the stool without evidence of the source being in the upper gastrointestinal tract.

## Conclusions

Proper education of the lay public to the importance of yearly complete physical checkups must be followed by a more alert medical profession primarily concerned with the early diagnosis of incipient cancer. The modern family physician is the logical "detective" in this program. He has at his command all of the simple essential diagnostic tools for visualizing fifty per cent of cancers. Through prompt referral to specialized fields when indicated he can complete the diagnosis in almost one hundred per cent of cases. Uniform standards for such a physical checkup for cancer can be developed with the focal point being the office of the family physician. Only then will the survival rate from cancer be altered for the better.

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2. Fentress, V., and Sandweiss, D. J.: Segal's tubeless gastric analysis with azure A resin compound; a simple procedure for screening individuals with achlorhydria in a gastric detection program.

*J. A. M. A.* 165:21-24, 1957.

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### KINESCOPE K16: CANCER DETECTION

This kinescope is available through your Division of the American Cancer Society. Running time: 38 minutes; 16-mm. color with sound.

Henry T. Randall, M.D.  
Clinical Director  
Memorial Center  
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George N. Papanicolaou, M.D.  
Professor (Emeritus) of Clinical Anatomy  
Cornell University  
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Emerson Day, M.D.  
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Prevention Clinic, Memorial  
Center, New York City

Genevieve Bader, M.D.  
Assistant Attending Physician  
Memorial Center  
New York City

The most effective weapons against cancer today are its detection in the early, asymptomatic stage, its immediate confirmatory diagnosis and its prompt effective treatment. One out of three cancer deaths could be prevented by use of the simple routine procedures of periodic health examinations available to every physician. Among the procedures illustrated in this kinescope, based on experience of more than 100,000 examinations, are the examinations of the head and neck, breast, abdomen and pelvis (including the Papanicolaou technique for the cytologic detection of cervical cancer)—all in a carefully systematized order with special attention to their practical use by the busy general practitioner.

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### KINESCOPE K 27: TUMORS OF CHILDHOOD

This kinescope is available through your Division of the American Cancer Society. Running time: 44 minutes; 16-mm. color with sound.

Harold W. Dargeon, M.D., Attending Pediatrician, Memorial Center;  
Associate Professor of Clinical Pediatrics,  
Cornell University Medical College and  
Members of the Attending Staff of Memorial Center

Dr. Dargeon and his associates indicate the important position occupied by neoplastic disease among our national child health problems and demonstrate that cures of many varieties of childhood cancer are possible. Valuable aids for eliciting the diagnosis and determining the management of tumors of childhood are presented.

Clinical histories and patients illustrate findings of physical examination, the role of biopsy, laboratory procedures and the significance of x-ray studies. Dr. Dargeon stresses the importance of the collaboration of clinician, pathologist and roentgenologist in the evaluation of diseases of childhood.

Examples of management by surgery, radiotherapy and chemotherapy are presented.

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# Geriatrics, Gerontology and Cancer

*Dean F. Davies, M.D., Ph.D.*

The great majority of the writings on the subject of geriatrics are directed toward the layman and are, for the most part, an assortment of common sense, tips on body hygiene and explorations of the workings of the elderly mind. As honorable as are the motives, the net effect is to create a new minority group. Our concern leads us to take care of this group by separating them from our homes and even community life, by improving the old people's homes and providing them with proper food and shelter. Some of these efforts are motivated by sheer political shrewdness. For the most part, however, the motives are of the highest order; the do-gooders are well-meaning. Nevertheless by identifying older adults as a community problem and by segregating them we may be doing them a disservice they might eventually openly resent and actively resist. Whether our methods of handling the problem are correct, the public is made vaguely aware of unmet needs. This is the first step.

## GERIATRICS AND CANCER

What are those needs? We are constantly reminded of the growing number of persons in the country past the age of 65. Reasoning runs something like this: Those past 65 are mostly retired. They need reassurance and something to keep them busy. They often have medical problems and the word "geriatrics" has been popularized to identify a branch of medicine which treats older people just as pediatrics treats children. At first blush this is a natural and proper development. Without considering geriatrics in its relation to medicine as a whole, there is good reason to take stock of its relation to the diagnosis and treatment of cancers.

During the period that geriatrics has

grown in popularity, the importance of age as a factor of concern in surgery has diminished. This has been repeatedly documented for all types of cancer. It is due less to specialization of the profession in the age group of the patients than to the improvement of surgical procedures for the organ system involved. Age, *per se*, plays a rapidly diminishing role in the surgical treatment of cancers. Oberhelman believes that "the surgical problems of the aged are scarcely more serious than those of persons in the younger age groups for the same conditions." Bricker, in discussing palliative surgery for carcinoma in the older age group at a meeting of the American Geriatrics Society, said that "we need not confine our thought to the elderly, because cancer surgery in them differs little from cancer surgery in general." Mortality rates for patients more than 70 years of age undergoing surgery for carcinoma do not appreciably exceed the mortality rate for patients less than 70 undergoing similar surgery.

The implied conclusion has been independently applied to gynecologic carcinoma by Morris. He states that "the principles of treatment are the same, regardless of age." He does not include age *per se* as a contraindication to treatment.

While a clear increase in operative mortality rate with age was found for pneumonectomy by Adams, this was associated with the physiologic status of the patients. He found that "when the reserves of the pulmonary, cardiac and vascular systems are relatively good, patients in the advanced age group may tolerate pulmonary resection as well as those of younger years and should not be denied surgery."

In analyzing the operative mortality of 276 patients over 70 years old who underwent major surgery for cancer over a sixteen year period, Anglem and Bradford found a decrease from 25.7 per cent in 1936 through 1940 to 13.3 per cent in

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521 West 57th Street, New York, New York.

1951 and 1952. They, too, felt that "the benefits of surgery should not be denied the elderly cancer patient on the basis of age alone." Gecht has taken the same point of view.

For the nonresectable cancers, radiotherapy can be used as easily in the elderly as in the young. In a panel discussion on palliation of advanced cancer in the older age groups, Uhlmann<sup>3</sup> had nothing to say about differences between radiotherapy in the young and the old.

Surely the "geriatric" aspect of the treatment of cancer is not urgently in need of a new branch of medicine. The improvements in treatment of cancer in the aged have resulted from the application of improved medical and surgical procedure rather than an increase in the number of physicians interested in geriatrics. On this basis there are some who believe that geriatrics has no role to play in medicine, that it is not comparable to pediatrics in that the diseases of the old are the same as the diseases of all adults.

### Early Diagnosis

What, then, is the role of geriatrics in cancer? There are four relatively neglected areas where the services of the physician are solely needed. One is that of diagnosis; in cancer this means *early* diagnosis. For cancer especially it means diagnosis before symptoms occur.

For many years there have been growing efforts to persuade the public to have routine periodic health examinations voluntarily. Many industries and other organizations have adopted the policy. In spite of these advances a small fraction of the potential benefit has been realized. The American Cancer Society has estimated that one-third of cancer cases are being cured. Realistic estimates of the cure rate possible with presently available diagnostic and therapeutic techniques run as high as 50 per cent. If true, there are some 40,000 additional persons with cancer who can be saved each year without relying on further research. This is a challenge to the physician interested in the older adult. This is where he can put his energy where

it will really count. Periodic screening for cancer should be started in the highest risk groups. In general these are in the "geriatric" age.

Figures 1 and 2 (p. 92) show the U.S. mortality distribution curves for men and for women in 1955 for total deaths and for cancer deaths. While the cancer mortality rate continues to rise throughout the lifespan, the greatest number of deaths from cancer occur between 65 and 70. This is below the age at which total mortality is at its peak. At what age the greatest number of curable cancers are discoverable by periodic examination can only be estimated, but the curves would indicate that the most rewarding results could be obtained by routine check-ups on men and women over 55. In the case of lung cancer, which accounts for a tenth of all cancer deaths in men, periodic screening should start at age 45. For cancer of the uterus and breast, which account for 39 per cent of female cancers, routine examinations should start at age 45 to include the major portion of the high-risk ages.

Table I (p. 94) shows incidence of leading forms of cancer in Connecticut<sup>4</sup> by sex in five-year intervals between 55 and 75 years. They represent approximately three-quarters of all cancers in the age group. The remainder are scattered sparsely among 18 major cancer sites of the body.

Examination for a particular type of cancer would be justified if a reasonable improvement in survival rates of such patients could be expected as a result of periodic checkups. In the absence of adequate information on this point, the practicing physician should assume that early diagnosis and treatment will help the patient. Data are accumulating on the value of early diagnosis (before symptoms) in each of the cancers listed in Table I. Table II shows selected survival rates experienced in Connecticut for the same cancers as listed in Table I. Among the major cancers, the five-year survival rates of localized cancers among men 55 to 74 years of age average about twice the rates observed

(Continued on page 93)





YOUTH — PAUL SAMPLE, NEW HAMPSHIRE



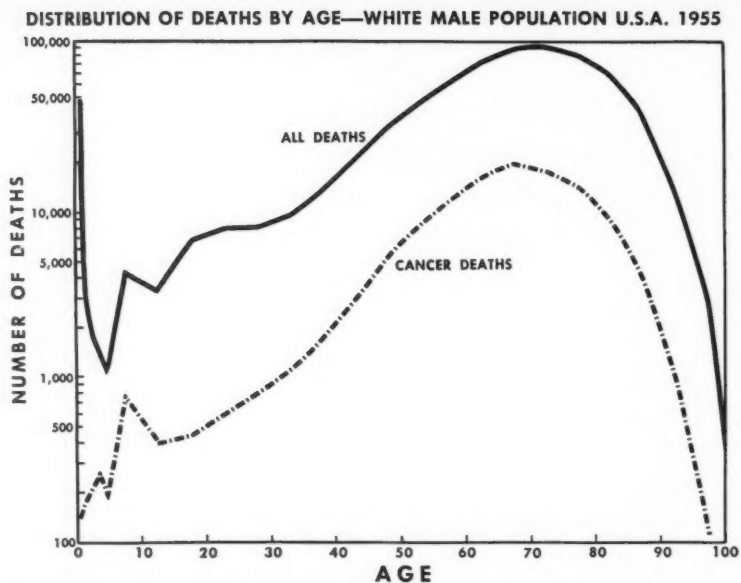


Fig. 1. Note: Deaths plotted on logarithmic scale

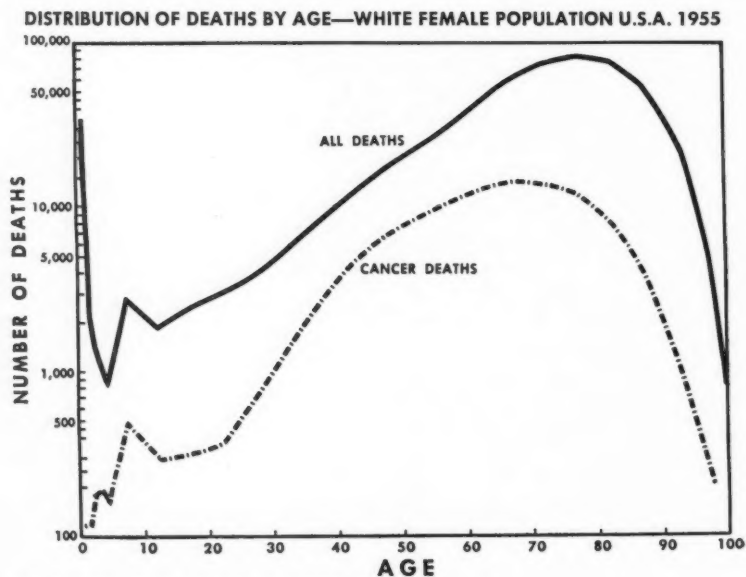


Fig. 2. Note: Deaths plotted on logarithmic scale

among those found to have regional spread. Those with distant metastases have a negligible five-year survival rate. Because of the low five-year survival rates it is not unreasonable to assume that many of the "regional spread" group actually had distant metastases at the time of classification and that many of the "localized" cancers had either regional or distant metastases. Assuming complete removal of the primary tumor, the only other explanation would be tumors of multicentric origin. Since those judged to be still localized at time of diagnosis have been discovered largely after the appearance of symptoms, it is reasonable to expect another considerable improvement in survival of those identified at a still earlier stage of the disease. A greater number of truly localized tumors would be expected in such a group.

This, then, is the first challenge to the geriatric physician interested in cancer—periodic checkups for presumably well patients. It is not easy and it is often thankless, but cancer, for the most part, is an insidious disease and it must be sought actively. A passive attitude too often results in tragedy.

### **Social Medicine**

The second challenge to the physician interested in older adults is to fill their void. The basis of the void needs no discussion. It has been described at great length in many writings. It is not a characteristic unique to the elderly, but it is more common among them. There are really only two components: a feeling of loneliness and a feeling of uselessness. They are easily recognized. Filling these voids cannot be accomplished by writing prescriptions for medicine, on the one hand, or by psychoanalysis on the other. The geriatric physician cannot divorce the health of the elderly patient from his relationship to his family and community. Geriatrics must be defined in terms broader than those conventional to medicine. The geriatrician must think in terms of the well-being of his patient rather than merely the absence of manifest disease.

What has this to do with cancer? There is evidence,<sup>11</sup> though admittedly not definitive, that cancers, along with many other diseases, are caused or aggravated by stresses and frustrations. Leshan and Worthington list four characteristics which have recurred in the literature describing the cancer patient: (1) the patient's loss of an important relationship prior to the development of the tumor; (2) the patient's inability to express successfully hostile feelings and emotions; (3) the patient's unresolved tension concerning a parental figure; and (4) sexual disturbance. The authors state that the loss of an important relationship has been reported by four authors to be the major finding in their cancer groups. It may be that ultimately attention to situational influences on the patient will be a recognized part of the armamentarium of the prevention and even the treatment of cancer. Unfortunately the case is not yet proved. In the meantime, the geriatrician should keep up with this growing literature.

For the patient who has or has had a cancer there may be years of suspense and waiting. Again, the treatment of pain or the routine checkup in search for metastases is wholly inadequate though all too often the extent of the service a physician supplies. The geriatrician should assume the responsibility of making the contacts for guidance on spiritual, vocational, hobby, club, rehabilitation or lodging needs that are indicated.

### **Preventive Medicine**

The third challenge of geriatrics to the physician is in taking his share of responsibility for preventive medicine. In the past, preventive medicine has been a function of a few state and federal government officials and industrial medicine. The practicing physician has not found it rewarding. Little has been known of how to prevent cancer. The possibility that periodic checkups actually prevent cancers by discovering premalignant lesions should not be underestimated.

In recent years, however, a clearer pic-

**Table I**  
Average Number of Cancer Cases Diagnosed in Connecticut—1947-1951

<b>Male</b>					
	<b>55-59</b>	<b>60-64</b>	<b>65-69</b>	<b>70-74</b>	<b>Total</b>
Large Intestine and Rectum	283	384	375	346	1,388
Bronchus and Lung	216	290	222	181	909
Stomach	173	225	255	232	885
Prostate*	84	157	231	306	778
Skin	176	184	177	196	733
Buccal Cavity and Pharynx	102	138	154	112	506
Bladder	71	110	129	103	413
TOTAL	1,105	1,488	1,543	1,476	5,612
ALL SITES	1,575	2,045	2,104	1,917	7,641
%	70.16	72.76	73.33	77.00	73.45
<b>Female</b>					
Breast‡	389	366	335	307	1,397
Large Intestine and Rectum	308	295	343	346	1,292
Uterus (total)**	310	297	226	144	977
Skin	117	138	144	151	550
Stomach	92	98	136	144	470
Ovary	98	92	73	64	327
TOTAL	1,314	1,286	1,257	1,156	5,013
ALL SITES	1,710	1,722	1,710	1,603	6,745
%	76.84	74.68	73.51	72.11	74.32

\* 329 cases at ages 75-79.

‡ 364 cases each at ages 45-49 and 50-54.

\*\* 229 cases at ages 40-44; 269 cases at ages 45-49; 324 cases at ages 50-54.

**Table II**  
Five-Year Survival Rates per Hundred Cases Diagnosed in Connecticut—1935-1951

<b>Male</b>							
	<b>55-64</b>		<b>65-74</b>		<b>All Ages</b>		<b>All Stages</b>
	<b>Loc.*</b>	<b>Reg.‡</b>	<b>Loc.*</b>	<b>Reg.‡</b>	<b>Loc.*</b>	<b>Reg.‡</b>	
Large Intestine	35.1	—	27.3	11.6	32.5	17.8	19.0
Rectum	31.8	14.6	17.2	—	24.1	14.3	15.4
Bronchus and Lung	5.7	2.9	—	—	3.2	3.1	2.0
Stomach	16.6	4.3	8.5	4.8	12.3	4.4	5.9
Prostate	35.5	—	28.1	19.0	24.4	19.0	19.5
Skin	76.7	—	61.9	—	67.0	—	64.2
Buccal Cavity and Pharynx	56.8	10.0	45.0	12.5	51.8	11.2	36.2
Bladder	32.4	—	26.4	—	32.4	—	25.9
ALL SITES	39.6	10.3	31.8	9.3	22.4	11.0	22.4
<b>Female</b>							
Breast	69.6	33.8	59.4	31.9	66.1	35.5	45.1
Large Intestine	42.3	28.4	29.3	21.0	37.8	22.6	23.6
Rectum	37.8	—	—	—	32.0	18.8	22.1
Uterus—Cervix	47.0	25.8	—	—	52.8	29.2	42.1
Body	71.5	—	39.4	—	64.7	38.3	57.0
Skin	82.5	—	70.7	—	73.9	—	70.9
Stomach	—	—	—	—	9.9	2.8	4.5
Ovary	—	—	—	—	50.8	18.9	22.2
ALL SITES	53.3	23.9	42.0	19.8	52.3	25.9	34.1

\*Localized. A localized cancer is one in which the neoplasm has not extended beyond the limits of the organ of origin or metastasized by other means.<sup>4</sup>

‡Regional. Regional involvement means that the neoplasm has extended to the local or regional lymph nodes, has spread by direct growth beyond the boundary of the specific primary site or has been implanted in some tissue within the same body cavity without involving another organ in that body cavity.<sup>4</sup>

ture of environmental causation factors of some of the cancers has been unfolding. For example, in two large-scale studies those who have stopped smoking cigarettes have had a lower mortality rate from lung cancer than those who continued to smoke. In the American Cancer Society study,<sup>8</sup> among 3,100 heavy smokers, 22 died of bronchogenic carcinoma (well-established cases of bronchogenic carcinoma exclusive of adenocarcinoma) but among over ten times as many (32,392) nonsmokers, only four died of the disease. Those who had stopped smoking more than a year prior to the beginning of the study had a lower lung cancer mortality than those who continued; the difference was statistically significant. The implications for preventive medicine in this disease, which accounts for the largest number of cancer deaths in men, are obvious. They are backed by extensive data on the pathogenesis of human lung cancer and by completely compatible experimental data in animals.

More notable were the results in total mortality from any cause. Other things being equal, among men in the 50-69 year age group the mortality rate of pack-or-more-a-day smokers was twice as high as for nonsmokers. The medical profession cannot afford not to seek out all of the facts concerning this relationship and act according to an objective appraisal of them.

Another example of an area deserving attention in preventive efforts is that of cervical cancer. There is a growing literature statistically associating cancer of the cervix with cervicitis, prostitution, marriage to uncircumcised males and a low incidence of cervical cancer in women whose husbands are generally circumcised (Jews, Fijis and Moslems) and in nuns.<sup>6,15</sup> Experimental evidence compatible with these associations has been obtained by Pratt-Thomas and co-workers who have demonstrated a stimulatory effect of human smegma on the cervico-vaginal epithelium of mice. Such data suggest that preventive medicine in cervical cancer may begin with circumcision and extend throughout life with close at-

tention to sex hygiene. Here, again, is one of the commonest types of cancer—the second most frequent site in American women—where the greatest contribution of geriatrics can be in prevention.

Concern for the aging and the aged leads naturally to a desire to improve their lot. In recent years the British have gone farther in geriatric medicine than we have in this country. Here there has been much discussion and some activity on social and psychologic problems of the older adult. Only a few professed geriatricians are active.

### GERONTOLOGY AND CANCER

Proper emphasis has not been placed on needed research on the influence of age in carcinogenesis. It is well known that the chronic diseases which are generally associated with aging cannot be wiped out by the expedient of identifying a new area of medicine. It takes research and more research to obtain answers to most of these problems. Thus, chronic bronchitis, orthopedic surgery and glycosuria—to name a few—have become the subject of chapters of a modern book on geriatrics. The differences between these diseases in the elderly and the rest of us are sometimes overplayed, sometimes ignored, depending on who writes the chapter.

The fact is that adult life, normal or diseased, is a continuum and there has rightly never been agreement on where aging begins. Some have said it starts at conception; others confine it to the years after retirement. However, no advantage is gained by such arbitrary distinctions.

From the earliest recorded history man has disliked dying. He wants to continue to live, but has always had cancers and cardiovascular and other diseases to contend with. These diseases, so common in later life, are being studied in laboratories concentrating on the respective disease states. In the meantime, a growing volume of data has shown that, in the absence of manifest disease, there are profound, though gradual, changes taking place during the aging process. These seem unrelated to pathologic states. They range

from a diminished blood flow through the kidney to the greying of hair. These are the outward manifestations of a process or processes associated in some way with the passage of time. There has been a great deal of speculation on the underlying causes of these changes with age. The fact is that they still belong in the great unknown. Numerous attempts have been made to interpret phenomena of aging in terms of curves of mortality rates plotted against age<sup>6,14</sup> but several fallacies in this type of approach have been pointed out.<sup>5</sup>

Nevertheless, there is good reason to believe that the increased incidence of disease and mortality with advancing years is tied up with the so-called normal changes associated with aging tissues. It is here that the gerontologist can contribute to the conquest of the diseases which point to the seeming loss of ability to resist or combat deviations from the "normal." It is for him to examine the body defenses against cancers at different ages to determine the cause of the rise in mortality rates with increasing age. Herein may lie a common denominator of all cancers. At least it will attack a vicious problem from an angle too long neglected.

What is the role of the practicing physician in this area? It is that of leadership in pointing out the problems for research which he sees in his practice. Surely the layman, whether on the street, in Congress or on the board of a voluntary health

agency does not see the urgent problems for research as well as the physician in practice. The science writer frequently takes over the crow's nest of the ship of medical research—and he often does a good job. But his orientation is toward fascinating the public and not toward the problems for which the physician has no answer.

It is the medical profession which is responsible for the health of the nation. It knows better than any other group how inadequate are the measures which can be called on to fight the diseases common to the older adult. This is especially true for cancer. The physicians sincerely interested in geriatrics wisely put their bets on gerontology, the science of aging, ultimately to provide the answers to combating the portion of disease associated with the process of aging. They become a pressure group for funds to support such research through established agencies, such as the American Cancer Society and those dedicated to research on aging.

## Summary

The relationship of cancer to geriatrics and gerontology has been discussed. In geriatrics arguments for emphasizing early diagnosis, preventive medicine, and social medicine are presented. The need for the support by physicians of vastly increased research in gerontology as it relates to cancer and other diseases is pointed out.

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# The Pediatric Aspects of Cancer

*Horst A. Agerty, M.D.*

Cancer and accidents now comprise the two leading causes of death in children beyond the age of two years. This increase is a relative one due to the success of public health prophylactic measures and the effectiveness of antibiotics in the prevention and treatment of infections.

Sarcomas far outnumber carcinomas in pediatric cases. Tumors seen in the first five years are usually of congenital origin. While they exist before birth, they are not recognized until later, when a clinical diagnosis becomes possible. Benign tumors are actually more frequent in early life. Many are hamartomas which are tumor-like congenital malformations resulting from overdevelopment of one or more tissue elements present at the site of the tumor, such as hemangiomas.

In the proper management of the cancers of infants and children, cooperation among pathologist, radiologist, surgeon and pediatrician is necessary. The chief means of treatment are surgery, chemotherapy and irradiation. While standard textbooks frequently give dire prognosis in some of these tumors, actually many of them offer a much more hopeful outlook than they did before the advent of newer methods of treatment.

The etiology of these tumors is still elusive. However, a number of interesting factors are known; for instance, teratoid tumors are found more frequently where there is a history of twinning. Another interesting observation is that malignant melanoma can be diagnosed histologically in children, whereas clinically it does not become malignant until after childhood has passed. Fifty per cent of all tumors in childhood occur in the first five years. After this, there occurs a drop in incidence, with a new rise after ten years of age. Infection may play a part in the etiology since in some cases the onset of a lymphoma appears to have

been preceded by bacterial infection.

Among the more common sites of cancer in the pediatric age group are the central nervous system, the eye, the kidneys, the adrenals, bone, soft tissue and hematopoietic system. At times the rapid progress of some neoplasms in early life may give rise to symptoms strongly suggesting an acute infectious process. For the most part, however, neoplasms in children reveal themselves as solid masses. For this reason, all solid masses palpated in infancy and childhood should be regarded as malignant neoplasms until histologic examination of the removed mass has revealed its exact nature.

## Tumors of the Central Nervous System

The highest incidence is in tumors occurring below the tentorium. The medulloblastoma is a rapidly growing, malignant glioma. The most common tumor is the astrocytoma. This grows slowly, often with a cyst contained within it. It usually occurs in the cerebellum. Next in frequency to astrocytoma and medulloblastoma among infratentorial tumors is the ependymoma. This tumor is usually found in the caudal portion of the fourth ventricle. Increased intracranial pressure is the most common finding. While the malignancy of this tumor is of relatively low grade, the location makes its removal hazardous and usually impossible. Roentgen therapy following the partial removal of the tumor, in an attempt to re-establish the spinal fluid circulation, is the usual method of therapy. Ingraham and Matson report five patients out of a group of nineteen alive from eight months to ten years after therapy.

Gliomas of the optic nerve and brain stem are also common. The most common supratentorial tumor is the craniopharyngioma. Symptoms in brain tumor are generally due to increased intracranial pressure, manifesting itself by bulging fon-

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tanelles, large open skull sutures, vomiting (especially worse in the morning), headache, stiffness of neck, diplopia, papilledema, disturbances of veins along the scalp and bradycardia. Roentgenogram may show erosion of the sella turcica and also the separation of sutures. Jacksonian convulsions, nystagmus, ataxia and ocular palsy are also important findings.

The definitive diagnosis is frequently made by means of air studies (ventriculograms) and the evaluation of the previously mentioned symptoms and signs. Therapy consists of complete removal wherever possible, otherwise radiation therapy is employed.

The prognosis varies with the tumor, being poor in medulloblastomas and quite good in astrocytomas, if the latter are removed in toto.

Spinal cord tumors are seen quite rarely in the pediatric age group. They may be benign or malignant. Symptoms will be due to spinal cord compression. Wherever possible the tumor is removed.

### **Intrathoracic Tumors**

Mediastinal tumors such as neuroblastomas are the most common ones seen. Primary malignant neoplasms of the thymus gland are quite rare, but the thymus gland may be involved in mediastinal lymphosarcoma, leukemia or Hodgkin's disease. Primary neoplasms of the lung are very rare. Sarcoma is seen more frequently than bronchogenic carcinoma. The clinical manifestations of lung tumor may suggest pulmonary infection. Teratomas in childhood may become teratocarcinomas in later life. Mediastinal tumors may be asymptomatic or give symptoms related to pressure of the mass on adjacent structures. Surgical removal is generally preferred, but irradiation should be combined with this or used alone where removal is not feasible.

### **Leukemia in Childhood**

Ninety-five per cent of childhood leukemia is of the acute variety. Since the cells cannot be specifically diagnosed, it is best to classify acute leukemia as stem-

cell leukemia. Anemia, fever, malaise and bone pains are some of the commonest symptoms and signs of leukemia. At the present time rather prolonged remissions up to several years may be hoped for in the treatment of acute leukemia. In this disease experimental chemotherapy has had a great field. The real hope in this disease at the present time seems to lie in finding a succession of agents which will control the process.

In the therapy of leukemia there are two major groups of compounds: (1) steroids and ACTH and (2) antimetabolites. Steroids and ACTH act rapidly and are utilized in acutely ill patients in whom a quick result must be obtained. The antimetabolites consist of three main groups: folic acid antagonists, purine and glutamine antagonists.

In the first group, amethopterin is especially useful. Mercaptopurine is a very valuable drug whose effect is obtained slowly, but which produces remissions slightly longer than those seen with the antifolic agents. The glutamine antagonists include azaserine. This is not valuable if used alone, but in combination with mercaptopurine may delay briefly development of resistance. Acute leukemia in children not treated with such specific agents has been associated with a median survival of four to five months. With the above named specific agents, the median survival is upwards of twelve months. The dosage of amethopterin is 2.5 mg. per day orally in a 5-year-old child; 6-mercaptopurine, 2.5 mg. per Kg. body weight per day orally. The dosage of cortisone divided into two to four daily portions varies from 50 to 200 mg. per day depending upon the patient's age and severity of symptoms. The dosage of corticotropin is 40 to 80 mg. per day. The dosage of the newer steroid drugs is proportionately less. It is noteworthy that during these remissions the child may appear to be unusually well and it is often difficult for the family to continue to accept the original diagnosis. Unfortunately, all this comes to an end.

In no type of tumor is the importance of sympathetic, unhurried presentation of

the problem more important than in dealing with acute leukemia. A study at the Memorial Hospital (New York) concerning the reaction of parents whose children were found to have leukemia showed how often these parents felt that the initial imparting of the diagnosis by the first physician was not satisfactory. The initial diagnosis was often described as "a blow." It was felt that the initial physician did not show sufficient sympathy and compassion and that he did not take sufficient steps to make available the best resources in the community which could be marshalled for the optimum treatment of the case.

### **Malignant Tumors of Bone**

Malignant osteogenic sarcoma, fibrosarcoma, chondroblastic sarcoma, Ewing's tumor, metastatic bone tumors from neuroblastomas, Wilms's tumors and lesions associated with leukemia are those most commonly seen. Symptoms are pain, swelling and disturbed functions of the extremities involved. In early stages, fever is rare except in Ewing's tumor. Steps in diagnosis consist of physical examination, roentgen-ray studies, blood studies, serology, blood chemistry and biopsy either by aspiration or direct surgical attack. Serum alkaline phosphatase is usually elevated in osteogenic sarcoma. Osteogenic sarcoma requires early amputation. Ewing's tumor is treated by irradiation alone. The reticulum-cell sarcoma is also treated by irradiation. The prognosis is fair in osteogenic sarcoma; 21 per cent of 265 patients were living after five years in a series at Memorial Hospital. The prognosis in Ewing's tumor is poor; a 4.1 per cent survival rate after five years in a series of 73 cases.

### **Neuroblastoma**

Neuroblastoma is usually seen during the third and fourth years of life. It originates in a simple neuroblast. It is widespread in location but most frequently found in a retroperitoneal area. This tumor may occasionally show a spontaneous regression by maturing into a ganglio-

neuroma. The tumor's usual course, however, shows it to be highly malignant and to metastasize early. A left-sided tumor spreads more frequently to the skull; the right-sided, to the liver. Neuroblastoma also metastasizes to the skeleton, lymph nodes and lung. The prognosis is usually serious but if diagnosis is early it may be somewhat better. The clinical course is often baffling. Headache, bone pains, intra-abdominal bleeding, an intra-abdominal mass, calcific shadows, hepatic enlargement and exophthalmos are some of the most common findings. The differential diagnosis usually includes Wilms's tumor, polycystic kidneys and hydronephrosis. Characteristic cells of this tumor may be found in the bone marrow, namely, the rosette formation. The optimum treatment of neuroblastoma is early and complete removal of the mass. Recently so-called massive attack on the tumor is being practiced in many centers wherein all possible metastases are removed, sacrificing portions of the involved viscera. Initial results have been encouraging. Antimetabolite therapy is being used in addition to radiation therapy after the surgical attack on the case. Spontaneous cures are rare, but early removal followed by irradiation has produced some cures. In general, the outlook is grave.

### **Tumors of the Kidney**

Wilms's tumor is embryoma of the kidney. This is one of the most common abdominal neoplasms of early life. Most of these tumors appear during the first five years. The tumor is usually unilateral; the presenting complaint is usually that of an abdominal mass. Fever and leukocytosis may be present if there has been hemorrhage and necrosis within the tumor. On examination, the mass is revealed as firm and non-tender and may extend to the midline and down into the iliac fossa. It does not commonly cross the midline. An intravenous pyelogram may show distortion of the renal pelvis. The neoplasm is encapsulated until late in its history, after which it may invade the renal pelvis and ureter. These cases should be considered

surgical emergencies and operated upon almost immediately. Palpation of the mass should be held to a minimum. After tumor removal, irradiation may be instituted. The recovery rate is up to 50 per cent in patients under one year of age, properly treated. After the age of one year, the prognosis is poorer. Metastases, when they do occur, usually appear within two years after the nephrectomy.

### Miscellaneous Tumors

Retinoblastoma is a relatively rare malignant tumor of the eye found almost exclusively in infants and young children. The onset is intrauterine. Treatment consists of enucleation. Carcinomas of the nasal pharynx and tonsils are rarely seen. Carcinoma of the thyroid has been reported and is said to be less rare than generally believed. Carcinoma of the liver, while relatively uncommon, must be considered in a differential diagnosis of abdominal masses. Rhabdomyosarcomas are described as originating in the prostate or bladder.

### Testicular Tumors

The most frequent neoplasm of the testis is the embryonal carcinoma, which is highly malignant and metastasizes widely, especially to the lungs. The chorionepithelioma is considered by some a variety of embryonal carcinoma. Therapy consists of excision and irradiation. Prognosis, while poor, is not hopeless.

### Ovarian Tumors

Carcinoma of the ovary is occasionally seen. Sarcoma botryoides is a rare neoplasm arising on the vaginal wall or cervix uteri. This is seen in the early years of life. It is associated with a foul discharge in the presence of multiple grapelike masses protruding into the vagina. The prognosis is grave. Treatment consists of early radical excision.

### Tumors of the Soft Tissues

Sarcomas of soft parts usually have a higher degree of curability in children than

in adults. Pack reports a 50 per cent recovery rate. It is important that, when muscles are removed, the involved muscle be excised entirely.

### Lymphosarcoma

Lymphosarcoma is a malignant neoplasm of lymphoid tissues. The presenting symptoms may be due to external lymphoid masses that are visible and palpable or to internal masses causing pressure on adjacent structures. At times a mass will be palpable in the abdomen (retroperitoneal). An acquired hemolytic anemia rarely occurs. Histologic study produces the definitive diagnosis. Roentgen therapy is perhaps still the most effective treatment. Nitrogen mustard and triethylenemelamine have also proved to be useful. No permanent recovery has been reported.

### Hodgkin's Disease

Clinically this may resemble lymphosarcoma. However, periods of high fever may occur (Pel-Ebstein's syndrome). Microscopically, the characteristic Reed-Sternberg cells are seen. Some cases run a long and chronic course, but no recoveries have been reported. Surgical removal, irradiation and triethylenemelamine therapy are the chief forms of treatment.

The alert physician, dealing with children, must constantly be aware of the possibility of neoplasms occurring in his patients. While proportionately, tumor patients make up a small percentage of an active pediatric practice, the relative importance of the cause of death makes tumors loom large in the minds of the parents. Careful physical examinations, attention to complaints, a high index of suspicion and painstaking studies will give satisfaction in that they will yield in many cases an early diagnosis which will make for optimum therapeutic results. Even in those cases where the ultimate outcome is fatal, the grateful parents will always remember that the acumen of their physician at least gave their child the optimum opportunity for cure.

[References available on request.]



# CANCER CLINIC

## Tumor Conference

The patient to be presented to this Clinic did not have cancer. He was treated for cancer because his disease was located in the stomach where benign and malignant processes are not easily distinguished. Except for the duration of his illness all the clinical features of this man's disease favored a malignant process and almost automatically led him to be treated for one. Few clinicians would have elected to do otherwise. His story raises a large problem, especially in geriatric practice.

**Case:** The patient is a fifty-six year old man who was admitted to this hospital on December 26, 1957 with the complaint of weakness and loss of appetite.

**Present Illness:** The patient described vague epigastric symptoms of pain for several years. He had been placed on an ulcer diet by his local doctor which he had followed sporadically since. About

three months prior to admission he began having rather marked epigastric pain in the right upper quadrant which was usually *postprandial*, often occurring immediately after eating. On several occasions this pain awakened him at night. He also described a fifteen-pound weight loss in the last three months. Examination by the patient's local doctor included an upper gastrointestinal series which showed a stomach ulcer, possibly malignant. The stomach had a good emptying time. One week prior to this hospitalization he had a gastric analysis showing achlorhydria.

**Past History:** The patient had an abdominal injury described as a crushing blow to his left lower abdomen about 1948. From that time he had rather intractable pain in the left upper quadrant. In 1951 he had an exploratory operation in another hospital at which time an enlarged spleen with many adhesions around it was encountered. A splenectomy was done at this time and the adhesions were divided. Following this procedure there

Presented by Talmage W. Nielsen, M. D., secretary, Tumor Conference Committee, and Ulrich R. Bryner, M. D., past-president of the Medical Staff, Wm. H. Groves Latter-Day Saints Hospital, Salt Lake City, Utah.

was little relief from pain and he had a second exploratory operation in August 1955, because of a persistent mass in the left lower quadrant. At that time the omentum was found to be attached to the anterior peritoneal wall, and the patient had a partial intestinal obstruction which was relieved. In December 1956, the patient was again complaining of left upper quadrant pain but no mass was palpated. He was again explored and a lysis of adhesions was done. In 1956 the patient was in an automobile accident and sustained a fracture to his right clavicle. The past history and review of systems were otherwise unremarkable.

*Physical Examination:* At the time of admission the blood pressure was 170/80 and the pulse regular at 84. The heart revealed a Grade I systolic murmur at the apex but was not enlarged to percussion. Abdominal examination showed a mass in the epigastrium which was thought to be separate from the liver. There was marked tenderness at the left costovertebral angle and in the left upper quadrant with some muscle guarding. Neurological examination revealed a loss of grip of the right hand and the patient described sensory paresthesias of numbness and tingling in the right upper extremity.

*Laboratory:* Blood showed hemoglobin 8.5 gm. or 54 per cent, leukocytes 9,950, 63 adult polymorphonuclears, 27 lymphocytes, 2 eosinophils, 7 monocytes, 1 basophil and 5 nucleated erythrocytes, and a few target cells were seen. Urinalysis was reported within normal limits. Occult blood was found in the stools on two occasions. Blood urea nitrogen was 13 mg. per cent, and alkaline phosphatase was 3.5 units. Liver studies revealed a total protein of 6.5 gm. per cent, 2.5 albumin, and 4.0 globulin. The A/G ratio was 0.6. The prothrombin time was 100 per cent. Serum bilirubin was 0.1 total, 0.05 mg. per cent direct and 0.05 mg. per cent indirect. Cephalin flocculation was negative. Thymol turbidity was 3.2 units. Upper gastrointestinal series showed a persistent irregularity in the antrum of the stomach which extended along the greater curvature and had a polypoid-appearing shadow. This

was interpreted as representing a carcinoma (Figs. 1-4). The chest film showed an increased density in the region of the right apex. An x-ray film of the patient's right clavicle showed marked separation of bony fragments and a piece of wire was found in the soft tissues of the left side of the neck.

*Hospital Course:* The patient was placed on ulcer diet and was treated with trisogel, probanthine and transfused with three pints of blood. Gastroscopic examination was also done and an antral ulcer was seen which was believed to be carcinoma. The patient was taken to surgery on January 7, 1958.

At operation the surgeon could not determine whether the lesion was benign or malignant. He seldom can. The previous crushing injury and the long standing ulcerative process produced adhesions that made recognition of tissue planes and characteristics a challenge. Such nodes as were seen were large and firm as was the mass around the ulcer. The surgeon could not tell what he was treating. He proceeded with his task of extirpating the lesion through these technical difficulties, a course to which he was committed before the incision was made. Errors in the diagnosis of gastric lesions can seldom be corrected at surgery even with gastrotomy and frozen-section biopsy. Occasionally a liver metastasis or lymph node will make the diagnosis of cancer clear, or some other clue will be discovered at operation. Nevertheless it is essentially the role of a surgeon in this situation to perform an operation that is adequate for cancer. Such surgery is often more radical and attended by a higher morbidity and mortality than would be required for a benign process. This is especially true when the lesion is high and the patient is elderly.

Such facts enjoin us to consider soberly whether one can safely avoid operation in gastric ulcer, or find a secure place for less radical surgical resections. Reports of cancer in an alarming percentage of patients giving a clinical picture of benign ulceration have appeared repeatedly in the literature to render the therapist uneasy and insecure in the conservative



Fig. 1

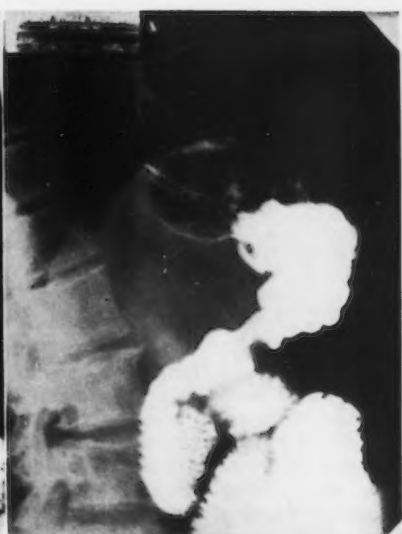


Fig. 2



Fig. 3



Fig. 4

Figs. 1-4. Films of the stomach at various angles of projection demonstrate an ulcer crater 1.2 cm. in diameter and 1 cm. in depth in the greater curvature of the antrum 2 cm. proximal to the pyloric canal. A persistent, abrupt contraction involved the lesser curvature opposite the lesion. The ulcer crater does not extend outward beyond the normal margins of the stomach. Considerable spasm deformity involves the antrum distal to the ulcer.



Fig. 5. The patient is well, at home and grateful for the relief that he has obtained from his chronic ulcer.

management of these cases. A representative series is that of Cain and his associates who studied 414 patients with benign-appearing gastric ulcers treated initially without surgery but followed for five years. Cancer was present or developed in 10.4 per cent of the entire group and was found in 24.3 per cent of the 140 patients who ultimately came to operation. Nine patients did not qualify for surgical exploration because of advanced disease and another nine patients were inoperable at the time of operation.

These figures are a bit disquieting and for many clinicians sufficient evidence to justify the stand that all gastric ulcers should come to operation radical enough to treat cancer. Such a course comfortably avoids the problems associated with diagnosis and diagnostic error, and unquestionably brings many patients to earlier and therefore more effective cancer therapy.

The real question, however, is how this balances out against the loss to life and health occasioned by the operation in light of the long-term surgical salvage.

The diagnostic error was estimated by our Radiology Department to be very small in the typical, punched-out, lesser-curvature ulcer with radiating mucosal folds and borders free of papillary projections. These cases when added to the instances of mixed and confusing x-ray patterns leave the error in the neighborhood

of 10 per cent as it is reported in the literature. Welch and Allen found 34 of 512 cases originally diagnosed as benign ulcer to have or to develop cancer subsequently. Of the ostensibly benign cases with resections as their initial treatment, 10.8 per cent had cancer. This left the absolute error between 6.6 per cent and 10.8 per cent and agrees substantially with an error of 9.8 per cent reported by Smith and Jordan. In the latter series the gastroscopist was wrong 26.8 per cent of the time. There is little comfort in any of these figures.

When one compares a 10 per cent risk of cancer (approximately 100 times that of the general population) with a surgical mortality that with modern techniques approaches 2 per cent, the case for surgery in gastric ulcer gains momentum. But what of the surgical morbidity? Some of our internists maintain that the instances of dumping, anorexia, distress, weight loss and loss of strength following operation justify the assumption of the 10 per cent risk when added to the 2 to 3 per cent mortality, especially since only 20 per cent of those with cancer resected will survive the operation five years.

In rebuttal our surgeons would remind their medical colleagues that the medical management of stomach cancer gives no hope whatever at present and the medical therapy of the benign gastric ulcer is far from illustrious.

In Cain's series of 336 cases selected for medical management at the Mayo Clinic only 22.6 per cent were considered to have done satisfactorily. Over 9 per cent of these patients developed cancer; 12 per cent had obstruction, hemorrhage or perforation and the remainder had recurrences and were refractory to medical measures. Results were worse the longer these patients were followed. Smith and Jordan claimed to salvage 60 per cent by conservative therapy but many of their cases were followed less completely or for shorter periods than those reported by Cain.

In contrast to this discouraging prospect 90 per cent of the 295 cases treated surgically in the series of Welch and Allen

remained well, 75 per cent were symptom free, 15 per cent had trivial symptoms which they were happy to accept in exchange for freedom from their ulcer distress. Only 10 per cent had the surgical morbidity our medical colleagues fear.

The success of surgery compares much more favorably with that of conservative management in gastric ulcer than is the case with duodenal ulcer where the threat of cancer is virtually non-existent. The two conditions should be kept separated in our thinking. In this hospital the majority viewpoint would seem to hold that surgical therapy should be given to all cases of gastric ulcer that would qualify as reasonable surgical risks except in those instances where prompt and permanent healing of the ulcer can be effected by medical programs or where duodenal ulcer coexists. Conservative resections are believed to have a place in the chronic ulcer which recurs repeatedly in the same place for years and fulfills x-ray and gastrosopic criteria for benignancy. In this

situation there would seem to be a local defect in the stomach wall which if left for sufficient time might become associated with malignant change analogous to that seen in the chronically inflamed cervix. Acid peptic digestion would appear to play a relatively minor role in these cases. Many of them secrete no free acid. Cancers were seen to develop five years after the initiation of therapy for clinically benign ulcers in five of Cain's cases and one made its appearance nine years after the first ulcer was diagnosed.

In all other cases where surgery is elected, the resection should remove at least two-thirds of the stomach together with the greater omentum and the gastro-hepatic ligament. Removal of the spleen and pancreatic tail are often indicated in the frankly malignant cases. Proximal resections as advocated by Sweet and his associates are probably preferable to total gastrectomy in the high-lying lesions whenever such a technique can be employed.

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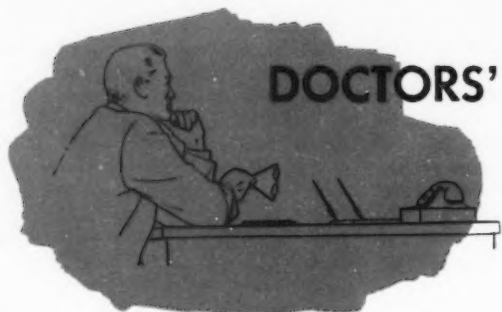
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### TWILIGHT MEDITATIONS

Fifty residents of a Home for Aged and Infirm were asked: "What is your main trouble?" Answers of 34 indicated somatic complaints, 16 denied having any trouble, six worried about another person, two complained only of age, one referred to lack of money, one to loss of memory and one longed for another interest. Replies to: "If you could have one wish, what would you wish for?" were: health 20, other person 14, nothing five, travel two, and one each — peace of mind, sex, leave here, stay here, adapt myself here, hear a symphony, wisdom, sleep, money, live life over.

Kahn, R. L.; Zeman, F. D., and Goldfarb, A. I.: Attitudes toward illness in the aged. *Geriatrics* 13:246-250, April, 1958.



## DOCTORS' DILEMMAS

**Q** *A 65-year-old man consulted me seven months ago for vague symptoms of indigestion, including anorexia, pain after eating and loss of weight. I referred him immediately for roentgenological studies. The roentgenologist assured me that the filling defect in the gastric wall indicated a benign ulcer and he suggested continuing medical treatment. Since that time weight loss has continued and the patient is clinically worse. Should the medical management be continued and, if so, how long?*

**A** Although roentgenographic examination is the most important method in the detection of gastric cancer it is not infallible. Roentgenologists today recognize the possibility of mistaking a cancerous for a benign peptic ulcer. Medical management has already been continued too long in this case; immediate exploratory laparotomy is indicated. Many instances of carcinoma in situ in gastric ulcers have been observed by critical pathologists, showing that cancer may develop on the basis of a chronic gastric ulcer. Such cancers are often mistaken for benign lesions and so managed until metastases make cure difficult or impossible. If cancer is disclosed by laparotomy in this case immediate resection is indicated.

**Q** *I have seen a recent statement in a lay magazine that the wax used in coating milk cartons of cardboard is a cancer-producing material. Should a doctor suggest to his patients that they no longer use*

*milk from these containers if milk in glass bottles is available? And what advice should be given when glass-bottled milk is not available?*

**A** The consultant to whom this question was referred stated that these containers are still used in his own household, but that the oil industries which furnish the petroleum waxes used for paraffinizing milk containers should undertake a comprehensive and competent study of the waxes furnished to the dairy industry, because tumors of the bladder have been produced in both rats and mice by English and American investigators following the implantation of paraffin pellets into this viscus. So-called fully refined paraffins vary in their chemical composition and their potentially carcinogenic properties. Legislative action is now under consideration to require carcinogenic studies of all food additives and of all substances used in manufacture of food containers. Until such studies prove the paraffins used for milk containers to be entirely noncarcinogenic, there remains the remote possibility of harm.

**Q** *In the excellent and well presented article by Dr. Combes (CA—Bull. Cancer Progr. 7:196, Nov., 1957), the statement is made that "no case of creosote cancer of the skin has been recorded in the United States." A case of multiple cutaneous carcinoma after creosote exposure is reported by Lenson in New England J. Med. 254:520, March 15, 1956.*

*In view of the fact that CA may be used for reference purposes in compensation cases, should not the statement, which appears to be in error, be corrected?*

**A** Dr. Combes had seen the Lenson report but could not accept the case to be of primary creosote etiology. The patient's 41 years exposure, as a painter, to lead and probably traces of arsenic and certainly to actinic rays, would appear to be a more probable primary etiologic factor than the comparatively short exposure to creosote. However, the old problem of multiple causes in biology arises here and it is possible that the superimposed creosote exposure had a contributory effect in the production of the carcinomatous lesions in the areas of chronic ulceration and infection. It is possible that similar scrutiny of the very few reports of cancer following exposure to creosote in the foreign literature would also reveal more likely primary etiologic factors. The extremely few cases of cancer—one in this country—reported among the thousands of workers handling creosote strongly suggest its innocence. Successful claim for compensation for skin cancer following exposure to creosote is unlikely. [It would be interesting to hear from other dermatologists and industrial physicians with patients who work with creosote.—Ed.]


**Q** *In CA, March 1957, page 39, it stated that the first indication of prostatic cancer is sometimes a stony-hard, asymptomatic nodule found at routine examination. This reminds me of the stony-hard calcifications by which one recognizes the normal prostate gland in histological section. Is there any correlation between physiological secretion of the prostate gland and the formation of calcified lumps and carcinoma in later years?*

**A** Although nodules found on routine rectal examination may occasionally turn out to be prostatic calculus or chronic nonspecific infection, the possibility of carcinoma must be kept in mind and ap-

propriate studies carried out. A roentgen-ray examination would help to localize a prostatic calculus. Prostatic massage might demonstrate prostatic infection but would not rule out a superimposed carcinoma for which appropriate biopsy studies would be necessary. In addition, serum acid phosphatase and prostatic acid phosphatase determinations would help in the diagnosis of prostatic carcinoma. Some observers have found exfoliative cytology with microscopic study of prostatic expressate for malignant cells of some help in the diagnosis of prostatic carcinoma. There is no known etiological relationship between the physiological secretions of the prostate gland and the formation of prostatic carcinoma in later years.

**Q** *A 57-year-old man complains of burning epigastric pain lasting an hour or two after meals. He has lost 18 pounds in weight over the past 10 months. His appetite is poor. There is no nausea or vomiting or blood in the stools. No abdominal mass is palpable. Gastroscopy was negative. Gastric content contains no free acid after histamine administration. Gastrointestinal series shows normal esophagus, stomach and duodenum. Two cytological examinations, using the gastric balloon, were positive—Class V and Class IV. A repeat gastrointestinal series is negative. Is exploratory laparotomy justified in this patient?*

**A** In spite of two negative gastrointestinal series and negative gastroscopy, the two frankly positive cytological tests not only justify but urgently demand laparotomy. The surgeon is almost certain to find a carcinoma that was hidden from the gastroscopist and the roentgenologist. In similar cases of positive cytology and negative gastroscopy and gastrointestinal series the lesion is often found just distal to the esophageal hiatus on the lesser curvature and posterior wall. The age of this patient should not be considered as a contraindication to exploration or resection. Under modern conditions of surgical procedure even older patients do well.



# new developments in cancer

## **Detecting Stomach Cancer . . .**

Dr. Cyrus E. Rubin of the University of Washington has found chymotrypsin lavage the simplest and most dependable method of detecting early stomach cancer. His technique has shown up nineteen of twenty cancers in one series. The procedure calls for withdrawing the contents of the fasting stomach through a narrow tube, pouring a pint or so of a solution containing chymotrypsin into the stomach, and, after ten minutes, withdrawing the solution and examining the sediment under the microscope. The chymotrypsin dissolves stomach mucus and loosens cancer cells. In expert hands, the test yields almost no false positives.

## **Auto-oxidation Inhibitor . . .**

Dr. Herbert M. Hirsch of the University of Minnesota has found that the body defends itself against the formation of carcinogens. He has discovered that normal cells and plasma contain AI, an auto-oxidation inhibitor that prevents the formation of free radicals which, a growing number of scientists feel, may be responsible for mutations and cancer. AI combines with the highly reactive free radicals and robs them of their ability to polymerize, Dr. Hirsch found. In one series of experiments, he showed that DOPA, which forms several free radicals in the process of being converted to melanin,

could be inhibited chemically by something in normal cells. That something is AI. DOPA was much less inhibited by cancer cells, however—apparently they were deficient in AI. Normal cell AI did not impede the DOPA-to-melanin transformation induced by ultraviolet rays, however. This indicated that AI acts upon enzyme systems “probably by combining with metal ions” involved in the chemical, but not physical, transformation of DOPA.

## **Indole a Carcinogen? . . .**

University of Miami scientists have found that the free radical, indole may be the key to carcinogenesis in one kind of rat liver cancer—the kind produced by feeding the animals 2AAF. Drs. W. F. Dunning and M. R. Curtis found that rats escaped 2AAF-induced cancer if they were maintained on a high casein diet. Casein lacks tryptophan, an amino acid which breaks down into indole. When indole in any of several forms was added to the diet the rats readily developed liver cancer. Indole exists in many forms. It is derived from the plant growth hormone, indole acetic acid, the hormone, adrenalin and the nerve substance, serotonin, as well as from tryptophan. The findings provoke speculation about the possibility of using agents which would bind free radicals and lessen the chances of the development of cancer.

time for the development of leukemia and doubled the incidence among mice.

Goldin (NCI) reports 3,5-dichloroamethopterin to be more effective against mouse leukemia than are other folic acid antagonists. Treated animals lived an average of 36.5 days; controls, 11.

Tocantins and others (Jefferson) irradiated 17 human leukemic patients (200-350 r) and infused homologous marrow with only fair therapeutic results. Marrow infusions are well tolerated. Marrow is obtained by extraction from ribs donated by public spirited citizens to a marrow bank. The marrow is infused within an hour of its extraction. Clinical results might be improved by higher dosages of marrow and radiation.

Friend (Memorial-SKI) reported that formalinized virus, as vaccine, protected 80 per cent, and as antigen for rabbit antiserum, 90 per cent, of mice against a specific leukemia. The antiserum had to be infused within an hour of the transplant.

Burchenal and associates (Memorial-SKI) obtained benefit in 20 per cent of patients with acute leukemia and lymphosarcoma, with spread to the meninges, by intrathecal injection of amethopterin.

Moloney (Holy Ghost-Tufts) found a basophilic elevation to from 3 to 5 times normal among Japanese survivors of atomic explosion a year or so before they develop leukemia. Fishman is exploring preleukemic enzyme changes.

Djerassi (Children's-Harvard) arrested thrombocytopenic bleeding in 70 per cent of cases by the use of platelets.

Ferrebee (Children's) with others at Cooperstown successfully stored marrow for safe human use by preserving it in glycerol at -110° F.

Furth and Metcalf (Children's) have detected a thymic lymphocytosis stimulating factor and found it to be elevated in the plasma of the leukemic mouse and of man.

Modest and Farber (Children's), in the research center where the usefulness of folic acid antagonists in leukemia was discovered, are producing and studying other antimetabolites, none of which has been found to be more effective than the older compounds.

Urbach (Roswell Park) found that patients with malignant lymphoma have four times the normal incidence of herpes zoster.

Pierce (U. of Chicago) reported that the leukemic

child who retains his defense against severe infection is able to control leukemia for a limited time. Two leukemic children in his series have complete and long lasting spontaneous remissions.

Good (U. of Minn.) found patients with Hodgkin's disease to have unusual tolerance for homologous skin grafts, and little resistance to diphtheria toxin, mumps virus, candida, etc.

Hyman (U. So. Calif) stated that 15 hospitals now cooperate in a national program to speed the evaluation of antileukemic compounds.

Dmochowski (M.D. Anderson) found similar particles in leukemic cells of man, mouse and chicken.

Stewart (NCI) produced tumors in hamsters with mouse leukemia filtrates.

Kit (M.D. Anderson) markedly depressed mouse lymphoma with 5-bromodeoxyuridine. This carefully conceived compound replaced thymidine equimolarly in DNA of E. coli and its phage and in tumor and spleen cells. It also inhibited the incorporation of formaldehyde and formate C<sup>14</sup> into DNA of rat thymus and the virus of mouse leukemia.

Ford (Tulane) found that mothers of leukemic children and of children with other cancers had pelvic irradiation during the third trimester of pregnancy more frequently than control mothers. Of the control mothers, 18.4 per cent had irradiation in the third trimester, of the mothers of leukemic children, 27.3 per cent, and of the mothers of children with other cancers, 29.5.

DeOme and others (U. of Calif.) report the tiny nodules on the breasts of mice to appear to be nests of viruses which later become cancers in more than one-half of the animals. The nodules grow, many becoming malignant, when transplanted with fat pads to the back of the mouse. About one-sixth of them revert to normal.

Richardson (U. of Wash.) found that Sprague-Dawley rats susceptible to cancer somehow transmit their susceptibility to induced hepatoma to resistant Long-Evans rats after the two had been housed in the same quarters for several months.

Cutting (Stanford) said there are "some rather surprising similarities" in the reproductive mechanisms of viruses and cancer. Several compounds, particularly the nucleic acid antagonists, which affect one will affect the other.

(To be continued in next issue.)

## COMING MEDICAL MEETINGS

<b>Date 1958</b>	<b>Meeting</b>	<b>City</b>
May 25-29	Air Pollution Control Association	Philadelphia
May 25-31	World Congress of Gastroenterology American Gastroenterological Association	Washington, D. C.
May 31-June 8	Congress of the International Association for the Study of the Bronchi	Wiesbaden, Germany
May 31-June 8	World Health Organization	Minneapolis
June 4-8	American Dermatological Association	Sun Valley, Idaho
June 9-13	American Nurses Association	Atlantic City
June 15-19	Canadian Medical Association	Halifax, N. S.
June 15-19	Third Canadian Research Conference, sponsored by the National Cancer Institute of Canada	Honey Harbour, Ont.
June 15-21	American Society of Medical Technologists	Milwaukee
June 16-18	American Neurological Association	Atlantic City
June 16-20	Gordon Research Conferences: Section on Proteins and Nucleic Acids	New Hampton, N. H.
June 17-19	American Goiter Association	San Francisco
June 18-22	American College of Chest Physicians	San Francisco
June 19-20	American Geriatrics Society	San Francisco
June 19-21	Endocrine Society	San Francisco
June 19-22	American Medical Women's Association	San Francisco
June 20-21	American Rheumatism Association	San Francisco
June 21	American Academy of Tuberculosis Physicians	San Francisco
June 21-22	American Diabetes Association	San Francisco
June 22-28	Congress of International Federation of Gynecology and Obstetrics	Montreal
June 23-27	American Medical Association	San Francisco
June 25-July 1	International Congress of Urology	Stockholm
June 29-July 3	American Proctologic Society	Los Angeles
July 1-3	Hawaiian Summer Medical Conference	Honolulu, T. H.
July 1-4	British Tuberculosis Association	London
July 6-12	7th International Cancer Congress	London
July 7-19	Southern Postgraduate Seminar	Saluda, N. C.
July 9-10	Rocky Mountain Cancer Conference	Denver
July 10-18	British Medical Association	Birmingham, England
July 15-21	Congress of Medical Women's International Association	London
July 16-23	International Union of Biological Sciences	London
July 21-23	Postgraduate Medical Association of South Texas	Houston
July 23-25	Thoracic Society	Copenhagen
Aug. 4-9	International Congress of Microbiology	Stockholm
Aug. 10-15	National Medical Association	Milwaukee
Aug. 11-16	World Federation of Occupational Therapists	Copenhagen
Aug. 12-24	4th World Assembly, Israel Medical Association	Tel Aviv and Jerusalem

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